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\* \* \* \* \* Welcome to STN International \* \* \* \* \*  
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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	AUG 15	CAOLD to be discontinued on December 31, 2008
NEWS	3	OCT 07	EPFULL enhanced with full implementation of EPC2000
NEWS	4	OCT 07	Multiple databases enhanced for more flexible patent number searching
NEWS	5	OCT 22	Current-awareness alert (SDI) setup and editing enhanced
NEWS	6	OCT 22	WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT Applications
NEWS	7	OCT 24	CHEMLIST enhanced with intermediate list of pre-registered REACH substances
NEWS	8	NOV 21	CAS patent coverage to include exemplified prophetic substances identified in English-, French-, German-, and Japanese-language basic patents from

2004-present

NEWS	9	NOV 26	MARPAT enhanced with FSORT command
NEWS	10	NOV 26	MEDLINE year-end processing temporarily halts availability of new fully-indexed citations
NEWS	11	NOV 26	CHEMSAFE now available on STN Easy
NEWS	12	NOV 26	Two new SET commands increase convenience of STN searching
NEWS	13	DEC 01	ChemPort single article sales feature unavailable
NEWS	14	DEC 12	GBFULL now offers single source for full-text coverage of complete UK patent families
NEWS	15	DEC 17	Fifty-one pharmaceutical ingredients added to PS
NEWS	16	JAN 06	The retention policy for unread STNmail messages will change in 2009 for STN-Columbus and STN-Tokyo
NEWS	17	JAN 07	WPIDS, WPINDEX, and WPIX enhanced Japanese Patent Classification Data

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,  
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items

NEWS IPC8        For general information regarding STN implementation  
of IPC 8

Enter NEWS followed by the item number or name to see news on that  
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\* \* \* \* \* STN Columbus \* \* \* \* \*  
\* \*

FILE 'HOME' ENTERED AT 18:02:17 ON 07 JAN 2009

=> FIL BIOSIS CAPLUS EMBASE		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.22	0.22

FILE 'BIOSIS' ENTERED AT 18:02:29 ON 07 JAN 2009

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FILE 'CAPLUS' ENTERED AT 18:02:29 ON 07 JAN 2009

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FILE 'EMBASE' ENTERED AT 18:02:29 ON 07 JAN 2009

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=> s MAPX

L1            13 MAPX

=> s MAPC

L2            294 MAPC

=> s 12 and recombinant

L3            6 L2 AND RECOMBINANT

=> dup rem 13

PROCESSING COMPLETED FOR L3

L4            3 DUP REM L3 (3 DUPLICATES REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L4    ANSWER 1 OF 3   BIOSIS    COPYRIGHT (c) 2009 The Thomson  
Corporation    on STN  
          DUPLICATE 1

AN 2008:88063 BIOSIS  
 DN PREV200800088197  
 TI Stem cells and embryonic stem cells: Biological differences.  
 Original Title: Celulas madre y celulas troncoembrionarias:  
 Diferencias  
 biologicas.  
 AU Riveros, Dolly Macias [Reprint Author]; Vazquez Chagoyan, Juan  
 Carlos;  
 Morales, Rogelio Alonso; Juarez, Marco Cajero  
 CS Univ Autonoma Estado Mexico, Fac Med Vet and Zootecnia, Program  
 Estudios  
 Avanzados Salud Anim, Km 15 5, Mexico City, DF, Mexico  
 marmac4@uaemex.mx; jcvvc@uaemex.mx; ralonsom@servidor.unam.mx;  
 cajeromarco@hotmail.com  
 SO Veterinaria Mexico, (OCT-DEC 2007) Vol. 38, No. 4, pp. 477-501.  
 CODEN: VTERBU. ISSN: 0301-5092.  
 DT Article  
 LA Spanish  
 ED Entered STN: 23 Jan 2008  
 Last Updated on STN: 23 Jan 2008  
 AB The stem cells have been classified in three types according to  
 their  
 natural niche of origin, aptitude and differential function:  
 totipotent,  
 pluripotent and multipotent; the first, called embryonic  
 stem cells  
 (ES) originate from the morulae; the second, come from the inner  
 cell mass  
 of the blastocyst (ICM); and the third, known as multipotent  
 adult  
 progenitor cells (MAPC) are found in some adult tissues. The  
 biological difference lies in their capabilities to produce cell  
 lines,  
 the totipotentials have the faculty to originate a complete  
 organism, the  
 pluripotent can generate all the cellular types and even the  
 germinal  
 line and the multipotentials can derivate in specific lineages.  
 The stem  
 cells are able to self-renew, and originate daughter-cells  
 compromised  
 with certain development routes; they are characterized for their  
 indefinite division and are morphologically and functionally  
 differentiated. When the stem cells and some progenitor types  
 are  
 extracted from their natural environment and are grown in vitro,  
 in  
 suitable medium, can be transfected and remain in an  
 undifferentiated  
 state without losing their potentiality; thus, when they are  
 reintegrated  
 to blastocyst receptors they are able to go on with their  
 development.

The study and compilation of information about these biological qualities of differential function, as well as their usefulness in homologous recombination and production of animal models that generate recombinant proteins, applicable for preventive-regenerating medicine and treatment of diseases, constitute the aim of this work.

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN  
 AN 2004:493864 CAPLUS  
 DN 141:66248  
 TI Homologous recombination in multipotent adult progenitor cells  
 IN Verfaillie, Catherine; Lakshmipathy, Uma  
 PA Regents of the University of Minnesota, USA  
 SO PCT Int. Appl., 70 pp.  
 CODEN: PIXXD2

DT Patent  
 LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.
WO 2004050859	A2	20040617	WO 2003-US38811
20031125			
WO 2004050859	A3	20040812	
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003298016	A1	20040623	AU 2003-298016
20031125			
US 20060228798	A1	20061012	US 2006-536716
20060530			
PRAI US 2002-429631P	P	20021127	

WO 2003-US38811 W 20031125

AB The invention relates to methods of altering gene expression by homologous recombination in a multipotent adult progenitor cell (MAPC). In particular, methods of producing a recombinant MAPC, of correcting a genetic defect in a mammal, of providing a functional and/or therapeutic protein to a mammal, and of transforming and differentiating a MAPC are provided. MAPCs containing an exogenous DNA as well as recombinant MAPCs and their differentiated progeny are also provided. The examples disclose gene targeting and genetic correction of a mutation in the FANCC protein, involved in Fanconi anemia, in mouse MAPCs, followed by transplantation of the corrected cells into FANCC-/- mouse and subsequent reversal of the FANCC deficiency.

L4 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN  
DUPLICATE 2

AN 2005:65444 BIOSIS

DN PREV200500061976

TI Activated protein C preserves functional islet mass after intraportal transplantation - A novel link between endothelial cell activation, thrombosis, inflammation, and islet cell death.

AU Contreras, Juan L. [Reprint Author]; Eckstein, Christopher; Smyth, Cheryl

A.; Bilbao, Guadalupe; Vilatoba, Mario; Ringland, Sharman E.; Young,

Carlton; Thompson, J. Anthony; Fernandez, Jose A.; Griffin, John H.; Eckhoff, Devin E.

CS 748 Lyons Harrison Res Bldg, 701 19th St S, Birmingham, AL, 35294, USA

juan.contreras@ccc.uab.edu

SO Diabetes, (November 2004) Vol. 53, No. 11, pp. 2804-2814. print. ISSN: 0012-1797 (ISSN print).

DT Article

LA English

ED Entered STN: 9 Feb 2005

Last Updated on STN: 9 Feb 2005

AB Clinical studies indicate that significant loss of functional islet mass

occurs in the peritransplant period. Islets are injured as a result of

detrimental effects of brain death, pancreas preservation, islet isolation, hypoxia, hyperglycemia, and immune-mediated events.

In

addition, recent studies demonstrated that islets are injured as  
 a result  
 of their exposure to blood and of activation of intrahepatic  
 endothelial  
 and Kupffer cells, resulting in inflammation and thrombosis.  
 Activated  
 protein C (APC) is an anticoagulant enzyme that also exerts  
 anti-inflammatory and antiapoptotic activities by acting  
 directly on  
 cells. Here, we report that exogenous administration of  
 recombinant murine APC (mAPC) significantly reduced loss  
 of functional islet mass after intraportal transplantation in  
 diabetic  
 mice. Animals given mAPC exhibited better glucose control,  
 higher glucose disposal rates, and higher arginine-stimulated  
 acute  
 insulin release. These effects were associated with reduced  
 plasma  
 proinsulin, intrahepatic fibrin deposition, and islet apoptosis  
 early  
 after the transplant. In vitro and in vivo data demonstrated  
 that  
 mAPC treatment was associated with a significant reduction of  
 proinflammatory cytokine release after exposure of hepatic  
 endothelial  
 cells to islets. mAPC treatment also prevented endothelial cell  
 activation and dysfunction elicited by intrahepatic embolization  
 of  
 isolated islets inherent to pancreatic islet transplantation  
 (PIT). This  
 study demonstrates multiple remarkable beneficial effects of mAPC  
 for PIT and suggests that A-PC therapy may enhance the  
 therapeutic  
 efficacy of PIT in diabetic patients.

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=> s Furcht/au
L5          0 FURCHT/AU

=> s l1 and Furcht
L6          0 L1 AND FURCHT

=> s l1 and homologous recombina?
L7          0 L1 AND HOMOLOGOUS RECOMBIN?

=> s l1 and homologous recombina?
L8          0 L1 AND HOMOLOGOUS RECOMBIN?

=> d his
  
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(FILE 'HOME' ENTERED AT 18:02:17 ON 07 JAN 2009)

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 18:02:29 ON 07 JAN 2009

L1 13 S MAPX  
L2 294 S MAPC  
L3 6 S L2 AND RECOMBINANT  
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)  
L5 0 S FURCHT/AU  
L6 0 S L1 AND FURCHT  
L7 0 S L1 AND HOMOLOGOUS RECOMBIN?  
L8 0 S L1 AND HOMOLOGOUS RECOMBIN?

=> s l2 and furcht

L9 0 L2 AND FURCHT

=> s l2 and homologous recombina?

L10 3 L2 AND HOMOLOGOUS RECOMBIN?

=> dup rem l10

PROCESSING COMPLETED FOR L10

L11 2 DUP REM L10 (1 DUPLICATE REMOVED)

=> d bib abs 1-

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L11 ANSWER 1 OF 2 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

DUPLICATE 1

AN 2008:88063 BIOSIS

DN PREV200800088197

TI Stem cells and embryonic stem cells: Biological differences.

Original Title: Celulas madre y celulas troncoembrionarias:

Diferencias

biologicas.

AU Riveros, Dolly Macias [Reprint Author]; Vazquez Chagoyan, Juan Carlos;

Morales, Rogelio Alonso; Juarez, Marco Cajero

CS Univ Autonoma Estado Mexico, Fac Med Vet and Zootecnia, Program Estudios

Avanzados Salud Anim, Km 15 5, Mexico City, DF, Mexico

marmac4@uaemex.mx; jcvvc@uaemex.mx; ralonsom@servidor.unam.mx;

cajeromarco@hotmail.com

SO Veterinaria Mexico, (OCT-DEC 2007) Vol. 38, No. 4, pp. 477-501.

CODEN: VTERBU. ISSN: 0301-5092.

DT Article

LA Spanish

ED Entered STN: 23 Jan 2008

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natural niche of origin, aptitude and differential function:

totipotential,

pluripotential and multipotential; the first, called embryonic stem cells

(ES) originate from the morulae; the second, come from the inner cell mass of the blastocyst (ICM); and the third, known as multipotent adult progenitor cells (MAPC) are found in some adult tissues. The biological difference lies in their capabilities to produce cell lines, the totipotentials have the faculty to originate a complete organism, the pluripotential can generate all the cellular types and even the germinal line and the multipotentials can derivate in specific lineages. The stem cells are able to self-renew, and originate daughter-cells compromised with certain development routes; they are characterized for their indefinite division and are morphologically and functionally differentiated. When the stem cells and some progenitor types are extracted from their natural environment and are grown in vitro, in suitable medium, can be transfected and remain in an undifferentiated state without losing their potentiality; thus, when they are reintegrated to blastocyst receptors they are able to go on with their development. The study and compilation of information about these biological qualities of differential function, as well as their usefulness in homologous recombination and production of animal models that generate recombinant proteins, applicable for preventive-regenerating medicine and treatment of diseases, constitute the aim of this work.

L11 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2004:493864 CAPLUS

DN 141:66248

TI Homologous recombination in multipotent adult progenitor cells

IN Verfaillie, Catherine; Lakshmipathy, Uma

PA Regents of the University of Minnesota, USA

SO PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.
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DATE

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PI WO 2004050859 A2 20040617 WO 2003-US38811  
20031125

WO 2004050859 A3 20040812  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,  
CA, CH,  
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TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
ZW  
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DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,  
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AU 2003298016 A1 20040623 AU 2003-298016  
20031125

US 20060228798 A1 20061012 US 2006-536716  
20060530

PRAI US 2002-429631P P 20021127  
WO 2003-US38811 W 20031125

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deficiency.

=> s multipotent adult stem cell or multipotent adult progenitor cell  
L12 170 MULTIPOTENT ADULT STEM CELL OR MULTIPOTENT ADULT  
PROGENITOR CELL

=> s l12 or l2  
L13 387 L12 OR L2

=> s l13 and recombinant  
L14 7 L13 AND RECOMBINANT

=> dup rem l14  
PROCESSING COMPLETED FOR L14  
L15 4 DUP REM L14 (3 DUPLICATES REMOVED)

=> d bib abs 1-  
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L15 ANSWER 1 OF 4 BIOSIS COPYRIGHT (c) 2009 The Thomson  
Corporation on STN  
DUPLICATE 1

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DN PREV200800088197

TI Stem cells and embryonic stem cells: Biological differences.  
Original Title: Celulas madre y celulas troncoembrionarias:  
Diferencias  
biologicas.

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Estudios

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 The study and compilation of information about these biological  
 qualities  
 of differential function, as well as their usefulness in  
 homologous  
 recombination and production of animal models that generate  
 recombinant proteins, applicable for preventive-regenerating  
 medicine and treatment of diseases, constitute the aim of this  
 work.

L15 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2006:1006474 CAPLUS

DN 145:369871

TI Stably transformed bone marrow-derived cells and uses thereof  
 for the

treatment or diagnosis of heart or vascular diseases

IN Aikawa, Ryuichi; Losordo, Douglas W.

PA Caritas St. Elizabeth Medical Center Boston, Inc., USA

SO PCT Int. Appl., 92pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.
DATE			

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PI	WO 2006102643	A2	20060928	WO 2006-US10981
	20060324			

	WO 2006102643	A3	20061116
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,  
 CA, CH,  
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
 GB, GD,  
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,  
 KP, KR,

MW, MX, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,  
SD, SE, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC,  
UZ, VC, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US,  
VN, YU, ZA, ZM, ZW  
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,  
HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR,  
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BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
AZ, BY,

KG, KZ, MD, RU, TJ, TM  
PRAI US 2005-665431P P 20050324  
US 2005-673305P P 20050419  
US 2005-735572P P 20051110

AB The invention provides compns. comprising genetically modified bone marrow

cells and related therapeutic and diagnostic methods.

Transduced bone

marrow cells can be therapeutically administered to a subject, such as a

human patient to provide for the expression of an encoded protein in the

subject in need thereof. In particular embodiments, the invention

provides a method for expressing a therapeutic (e.g., IGF-1 or human

growth hormone) or reporter gene in a cardiac tissue or a blood vessel of

a host subject through hematopoietic stem cells stably transformed with a

recombinant adeno-associated viral vector for the treatment or diagnosis of heart or vascular diseases.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2004:493864 CAPLUS

DN 141:66248

TI Homologous recombination in multipotent adult progenitor cells

IN Verfaillie, Catherine; Lakshminpathy, Uma

PA Regents of the University of Minnesota, USA

SO PCT Int. Appl., 70 pp.

CODEN: PIXXD2

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LA English

FAN.CNT 1

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

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PI WO 2004050859 A2 20040617 WO 2003-US38811  
 20031125

WO 2004050859 A3 20040812

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,  
 CA, CH,  
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
 GB, GD,  
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,  
 KZ, LC,  
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
 NI, NO,  
 NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,  
 SY, TJ,  
 TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
 ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW,  
 AM, AZ,  
 BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,  
 DK, EE,  
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,  
 SI, SK,  
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
 SN, TD, TG

AU 2003298016 A1 20040623 AU 2003-298016  
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US 20060228798 A1 20061012 US 2006-536716  
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AN 2005:65444 BIOSIS  
DN PREV200500061976  
TI Activated protein C preserves functional islet mass after  
intraportal  
transplantation - A novel link between endothelial cell  
activation,  
thrombosis, inflammation, and islet cell death.  
AU Contreras, Juan L. [Reprint Author]; Eckstein, Christopher;  
Smyth, Cheryl  
A.; Bilbao, Guadalupe; Vilatoba, Mario; Ringland, Sharman E.;  
Young,  
Carlton; Thompson, J. Anthony; Fernandez, Jose A.; Griffin, John  
H.;  
Eckhoff, Devin E.  
CS 748 Lyons Harrison Res Bldg, 701 19th St S, Birmingham, AL,  
35294, USA  
juan.contreras@ccc.uab.edu  
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and Kupffer cells, resulting in inflammation and thrombosis.  
Activated  
protein C (APC) is an anticoagulant enzyme that also exerts  
anti-inflammatory and antiapoptotic activities by acting  
directly on  
cells. Here, we report that exogenous administration of  
recombinant murine APC (mAPC) significantly reduced loss  
of functional islet mass after intraportal transplantation in  
diabetic  
mice. Animals given mAPC exhibited better glucose control,  
higher glucose disposal rates, and higher arginine-stimulated  
acute  
insulin release. These effects were associated with reduced  
plasma  
proinsulin, intrahepatic fibrin deposition, and islet apoptosis  
early  
after the transplant. In vitro and in vivo data demonstrated  
that

mAPC treatment was associated with a significant reduction of proinflammatory cytokine release after exposure of hepatic endothelial cells to islets. mAPC treatment also prevented endothelial cell activation and dysfunction elicited by intrahepatic embolization of isolated islets inherent to pancreatic islet transplantation (PIT). This study demonstrates multiple remarkable beneficial effects of mAPC for PIT and suggests that A-PC therapy may enhance the therapeutic efficacy of PIT in diabetic patients.

=> d his

(FILE 'HOME' ENTERED AT 18:02:17 ON 07 JAN 2009)

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 18:02:29 ON 07 JAN 2009

```
L1      13 S MAPX
L2     294 S MAPC
L3       6 S L2 AND RECOMBINANT
L4       3 DUP REM L3 (3 DUPLICATES REMOVED)
L5       0 S FURCHT/AU
L6       0 S L1 AND FURCHT
L7       0 S L1 AND HOMOLOGOUS RECOMBIN?
L8       0 S L1 AND HOMOLOGOUS RECOMBIN?
L9       0 S L2 AND FURCHT
L10      3 S L2 AND HOMOLOGOUS RECOMBIN?
L11      2 DUP REM L10 (1 DUPLICATE REMOVED)
L12     170 S MULTIPOTENT ADULT STEM CELL OR MULTIPOTENT ADULT
PROGENITOR C
L13     387 S L12 OR L2
L14       7 S L13 AND RECOMBINANT
L15      4 DUP REM L14 (3 DUPLICATES REMOVED)
```

=> s l13 and homologous recombina?

```
L16      3 L13 AND HOMOLOGOUS RECOMBIN?
```

=> dup rem l16

PROCESSING COMPLETED FOR L16

```
L17      2 DUP REM L16 (1 DUPLICATE REMOVED)
```

=> s hematopoietic stem cell

```
L18     51155 HEMATOPOIETIC STEM CELL
```

=> s l18 and homologous recombina?

```
L19      78 L18 AND HOMOLOGOUS RECOMBIN?
```

=> dup rem l19

PROCESSING COMPLETED FOR L19

```
L20     64 DUP REM L19 (14 DUPLICATES REMOVED)
```

=> s 120 and py<=2002  
L21 24 L20 AND PY<=2002

=> d bib abs 1-  
YOU HAVE REQUESTED DATA FROM 24 ANSWERS - CONTINUE? Y/(N):y

L21 ANSWER 1 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN  
AN 2003:356518 BIOSIS  
DN PREV200300356518  
TI Cooperating Mutations Are Necessary for the Development of AML in Mll-ELL Knock-In Mice.  
AU Luo, Roger T. [Reprint Author]; Kebriaei, Partow [Reprint Author]; Kaberlein, Joseph J. [Reprint Author]; Thirman, Michael J. [Reprint Author]  
CS Hematology/Oncology, University of Chicago, Chicago, IL, USA  
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 508. print.  
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)  
LA English  
ED Entered STN: 6 Aug 2003  
Last Updated on STN: 6 Aug 2003  
AB The (11;19)(q23;p13.1) translocation in acute leukemia results in the generation of a chimeric MLL-ELL fusion protein. To determine the consequences of expression of MLL-ELL in hematopoietic cells, we used homologous recombination in murine embryonic stem cells to generate an Mll-ELL knock-in allele. Although Mll-ELL chimeric and heterozygous mice express the Mll-ELL fusion gene, none developed acute leukemia spontaneously. Serial blood counts and smears from chimeric and heterozygous mice were analyzed monthly for 2 years with no apparent hematopoietic phenotype. In contrast, we previously reported that all mice transplanted with hematopoietic cells transduced with an MLL-ELL



retrovirus developed AML with a latency of 4-6 months. To determine whether a cooperating mutation was necessary to induce leukemia, a cohort of 10 heterozygous mice was treated with a single sublethal dose of N-ethyl-N-nitrosourea (ENU) at 100 mg/kg. As controls, wildtype littermates were treated with the same dose of ENU, and a second cohort of heterozygous mice was observed without ENU treatment. After 11 months of observation, 7 of 10 Mll-ELL knock-in mice treated with ENU have died from AML. None of the mice from either control group has developed leukemia or another malignancy. The morphologic appearance and flow cytometric analyses of the Mll-ELL leukemia cells were consistent with a monocytic or myelomonocytic phenotype, similar to that observed in patients with the (11;19)(q23;p13.1) translocation and in mice transplanted with hematopoietic cells retrovirally transduced with MLL-ELL. MLL-ELL is the first MLL chimeric fusion protein that results in the development of AML in both transplantation and knock-in mouse models of leukemia. Taken together, these data suggest that in addition to MLL-ELL, a cooperating mutation is necessary to induce acute leukemia. The contrast between the 2 models in the requirement for ENU to induce leukemia may be due to differences in the expression of the MLL-ELL chimeric protein, with expression driven by the retroviral LTR in the transplant model and by the endogenous murine Mll promoter in the knock-in model. Alternatively, the lack of the requirement for ENU in the retroviral transduction and transplantation model suggests that insertional mutagenesis by retroviral integration may provide a cooperating mutation necessary for leukemogenesis.

telomere length in mice.

AU Manning, E.; True, J.; Henckaerts, E.; Snoeck, H.; Geiger, H.;  
de Haan,  
G.; Lu, L.; Williams, R.; Van Zant, G.

SO Experimental Hematology (Charlottesville), (June, 2002) Vol. 30,  
No. 6 Supplement 1, pp. 112. print.  
Meeting Info.: 31st Annual Meeting of the International Society  
for  
Experimental Hematology. Montreal, Quebec, Canada. July 05-09,  
2002.  
CODEN: EXHMA6. ISSN: 0301-472X.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 24 Jul 2002  
Last Updated on STN: 24 Jul 2002

L21 ANSWER 3 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson  
Corporation on STN

AN 2002:241252 BIOSIS

DN PREV200200241252

TI Selectin-ligand pairs mediate the early phases of stem cell  
transplantation.

AU Fuller, Jennifer A. [Reprint author]; Kale, Sujata; Kelly,  
Robert J.;  
Lowe, John B.; Long, Michael W.

CS Immunology Program, University of Michigan, Ann Arbor, MI, USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 475a.  
print.  
Meeting Info.: 43rd Annual Meeting of the American Society of  
Hematology,  
Part 1. Orlando, Florida, USA. December 07-11, 2001. American  
Society of  
Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 17 Apr 2002  
Last Updated on STN: 17 Apr 2002

AB Knowledge regarding the molecular events of hematopoietic  
stem cell (HSC) homing during bone marrow transplant  
(BMT) is limited. The process of stem cell transplantation is  
reminiscent  
of that by which leukocytes trafficking into sites of  
inflammation in  
which selectin/ligand pairs tether leukocytes to activated  
vascular  
endothelium. We reasoned that for HSC to home to the bone  
marrow, they  
must first roll on E- and P-selectins constitutively expressed  
on bone

marrow endothelial cells. Selectin-ligands are active only when modified post-translationally by fucosylated oligosaccharide moieties represented by the sialyl Lewisx (sLex) tetrasaccharide determinant and its structural variants. Synthesis of such sialylated, fucosylated glycans is controlled by the lineage-specific expression of one or more distinct  $\alpha(1,3)$  fucosyltransferases (FucTs). Only two  $\alpha(1,3)$  FucTs, termed FucT-IV and FucT-VII, are expressed in leukocytes and their progenitors, and thus, control leukocyte selectin-ligand activity via  $\alpha(1,3)$  fucosylation.

To address the role of selectin-ligands in BMT, we used mice made null for fucosyltransferase-IV (FucT-IV), -VII (FucT-VII), or both (DKO) by homologous recombination that are congenic with their C57Bl/6 recipients. We first performed homing assays in which bone marrow non-adherent, low density (NALD) cells from FucT-null mice were transplanted into irradiated wild type (WT) mice. Donor cells were PKH26-stained and injected into the retro orbital sinus. At 3 hours post-injection, bone marrow, spleen and peripheral blood were examined by flow cytometry for the presence of PKH26+ cells. These data demonstrate a significant reduction in the seeding efficiency of FucT-IV, FucT-VII and DKO mouse cells (>twofold;  $p=0.04$ ) into WT marrow. In previous studies, we demonstrated a profound transplantation defect in the FucT-VII-null and FucT-DKO HSCs, with only 30 and 15% of the animals engrafting at limiting cell dilutions, respectively (Kale, et al., ASH abstracts 1999).

In order to determine whether HSC: selectin interactions are physiologically relevant (i.e., are not related to irradiation-induced inflammation and selectin-upregulation), we constructed parabiotic animals in which a WT and FucT-VII animal are conjoined. These parabiotic animals showed complete anastomosis in their blood supplies within one week. After six

weeks of parabiosis, a genotypic analysis of HSC progeny (i.e., hematopoietic progenitor cells; HSP) indicates that a FucT-mediated hematopoietic defect exists within the FucT-VII-null animals' bone marrow. Genotyping of individual HSC-derived hematopoietic colonies showed that the distribution between WT and null HPC in the marrow of the parabiotic WT animal is approximately 50% null and 50% WT whereas, in the bone marrow of the FucT-VII-null animals, 100% of the colonies are of the FucT-VII-null genotype. In summary, under myeloablative conditions, FucT-null HSC show a marked decrease in homing capacity and a profound transplantation defect. In non-irradiated parabiotic animals, FucT-positive cells (from the WT side) cannot enter FucT-null marrow as null animals' endothelial cells fail to express selectin-ligands. In contrast, FucT-null cells (that express selectins but not selectin-ligands) can enter WT animals' marrow in which the endothelial cells constitutively express selectin-ligands. We conclude that interactions between the carbohydrate Lex/sLex/VIM2 structures and constitutively expressed selectins in bone marrow venules play an essential role in HSC homing and engraftment.

L21 ANSWER 4 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson

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AN 2002:241171 BIOSIS

DN PREV200200241171

TI Targeting of CD34+ cells within the bone marrow for inducible transgenic

expression of cre recombinase.

AU Huettnner, Claudia S. [Reprint author]; Radomska, Hanna S.

[Reprint

author]; Okuno, Yutaka [Reprint author]; Nagy, Andras; Tenen, Daniel G.

[Reprint author]

CS Hematology/Oncology, Harvard Institutes of Medicine, Boston, MA, USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 454a-455a. print.

Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,

Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of

Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 17 Apr 2002  
Last Updated on STN: 17 Apr 2002  
AB The human CD34 gene encodes a type I transmembrane glycoprotein, which is expressed among other cells on early progenitor cells/stem cells in the bone marrow. Expression of the CD34 antigen decreases as hematopoietic stem cells differentiate and it is absent on all mature blood cells. We isolated the human CD34 locus from a human PAC library and had characterized and evaluated this genomic fragment for the expression of human CD34 as a reporter gene in stable cell lines and subsequently in several founder lines of transgenic mice. This fragment spanning 112 kb of the 5-flanking region and 24 kb of the 3- flanking regions of the CD34 gene was found to be sufficient for the expression of the human CD34 gene in the bone marrow and other tissues of transgenic mice. Moreover, the mRNA expression pattern of the exogenous gene was found to be similar to that of the endogenous murine CD34 gene in all tissues examined. FACS analysis demonstrated that expression of CD34 decreases with maturation of the cells. Three CD34 positive cell populations within the transgenic bone marrow were identified: hCD34+/mCD34-, hCD34+/mCD34+ and hCD34-/mCD34+. We have transplanted purified fractions of these cells (described in Okuno et al.) and found that bone marrow cells expressing the human CD34 transgene contain hematopoietic stem cells with long-term reconstitution activity, while they are not contained in the cell population expressing the endogenous murine CD34 gene. In order to determine if the elements enclosed within this PAC clone are sufficient for driving the expression of heterologous genes, we used homologous recombination in bacteria to modify the construct by inserting the sequence of the transactivator protein tTA, which is part of the tetracycline responsive expression system. The

plasmid was linearized and the construct was injected into fertilized murine oocytes. Animals transgenic for this construct termed CD34tTA were cross bred with mice that carry the gene for are recombinase under control of a tetracycline responsive element (TRE-cre). Expression of transresponder cre gene in this transgenic system will be suppressed in the presence of tetracycline, while in the absence of the antibiotic expression will be induced. Analysis of double transgenic animals by Northern Blot demonstrated cre expression in the heart, lung and the lymph nodes 5 days after withdrawal of tetracycline, consistent with expression of CD34 mRNA in the transgenic mice. As the human CD34 transgene is expressed in only a few percent of bone marrow cells, we were unable to detect cre mRNA expression by northern Blot, but could easily do so by quantitative real Time PCR analysis. The expression in the heart was determined to be more than seven-fold higher than in the bone marrow. The lowest expression was seen in the liver in concordance with our data generated by analyzing mice transgenic for the native CD34 locus. The results are of particular interest as they show that the 160 kb expression construct allows the targeting of CD34 positive cells within the bone marrow and controlled expression of heterologous transgenes. The CD34tTA-TRE-cre mice will allow for specific knock out of genes in CD34+ cells thus helping to elucidate the role of specific genes in hematopoietic stem cells. Moreover, controlled expression in CD34+ cells is important for experiments addressing the expression of heterologous genes in stem cells, which may ultimately find applications in gene therapy.

high level expression in hematopoietic cells of transgenic mice.

AU Meek, Sally C. [Reprint author]; Graubert, Timothy A. [Reprint author]

CS Internal Medicine, Division of Oncology, Section of Stem Cell Biology,  
Washington University School of Medicine, St. Louis, MO, USA

SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 663a.  
print.

Meeting Info.: 42nd Annual Meeting of the American Society of Hematology.  
San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 4 Jul 2001  
Last Updated on STN: 19 Feb 2002

AB To develop a system for targeting expression of genes to the hematopoietic stem cell compartment, we employed Sca-1 (Ly-6A/E), a well-characterized marker of murine hematopoietic stem cells. We assembled a targeting vector consisting of  
5.2 kb of Sca-1 genomic sequence isogenic to our embryonic stem (ES) cell  
line (129/SvJ strain, Ly-6A.2 allele). An enhanced green fluorescent  
protein (GFP) cDNA (Clontech Labs, Palo Alto, CA) was inserted immediately  
following the Sca-1 Kozak sequence in exon II. We removed the Sca-1  
initiation codon and left the remaining genomic sequences intact. A  
LoxP-flanked PGK-Neo cassette was subcloned downstream of the GFP reporter. As an initial test of this construct, we  
electroporated it into  
EL-4 cells, a murine B cell line that constitutively expresses high levels  
of Sca-1. A small fraction (0.5-1.5%) of transiently transfected cells  
demonstrated detectable GFP expression. A wide range of GFP activity was  
evident in stable clones, suggesting that our targeting construct is  
capable of directing high level expression after random integration into  
hematopoietic cells. We then electroporated this construct into  
RW4 ES  
cells and identified three clones that had undergone homologous recombination. One of these clones was transiently transfected with a plasmid encoding the Cre recombinase. We derived twelve correctly

targeted clones which had undergone excision of the PGK-Neo cassette. At this time, data is available from analysis of five chimeric founders obtained by injection of C57BL/6 blastocysts with one of the PGK-Neo (+) clones. Flow cytometric analysis of peripheral blood using the Ly-9.1 congenic marker demonstrated ES cell-derived hematopoiesis in a large proportion of leukocytes (range 31.8-73.6%) in these chimeric mice. GFP+ cells are easily detectable in peripheral blood from each of the animals, indicating that the Sca-1 targeting strategy successfully marked hematopoietic cells. The frequency of GFP+ cells correlates well with the degree of 129/SvJ chimerism and is surprisingly high (range 58.8-68.2% of ES-derived hematopoietic cells). However, approximately half of the GFP+ cells in each animal are Sca-1 negative, suggesting either increased post-transcriptional stability of the GFP reporter relative to the endogenous Sca-1 allele, or that expression of the targeted allele is dysregulated (possibly due to the retained PGK-Neo cassette). Analysis of F1 heterozygous mice (+/-PGK-Neo) should allow us to evaluate whether this system provides a valid strategy for genetically targeting hematopoietic stem cells in vivo.

L21 ANSWER 6 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2000:396218 BIOSIS

DN PREV200000396218

TI Molecules controlling hematopoietic development in vertebrates.

AU Cortes, Fernando; Labastie, Marie-Claude [Reprint author]

CS Institut d'Embryologie Cellulaire et Molculaire, Cnrs UPR 9064,  
49 bis,

Avenue de la Belle-Gabrielle, 94736, Nogent-sur-Marne Cedex,  
France

SO M-S (Medecine Sciences), (Feb., 2000) Vol. 16, No. 2, pp.  
198-204. print.

ISSN: 0767-0974.

DT Article

General Review; (Literature Review)

LA French

ED Entered STN: 13 Sep 2000



Last Updated on STN: 8 Jan 2002

AB Hematopoiesis first emerges in the embryo in the extra-embryonic mesoderm

in the yolk sac, and generates primitive erythoblasts.

Definitive

hematopoiesis then takes place in the fetal liver and bone marrow probably

after the seeding of stem cells migrating from the para-aortic region.

The analysis of the phenotype of mutant mice created by homologous

recombination in ES cells has led to the identification of mastegenes controlling hematopoietic development. These encode two types

of molecules, growth factors and transcription factors. Each appears to

act at a very timely defined stage of stem cell development, either to

specify the transition from the mesoderm to the hematopoietic differentiation, or the choice between the lymphoid or myeloid pathway, or

to trigger the proliferation of defined progenitors. A hierarchy in the

activity of these genes has been proposed based on results of knock-out

experiments: in the absence of some of these molecules, hematopoiesis

completely fails to occur, whereas the lack of others only compromises the

development of one pathway. The ongoing challenge is now to unravel the

downstream signalling pathways used by these growth and transcription

factors to influence hematopoietic stem cell decisions.

L21 ANSWER 7 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 1999:394228 BIOSIS

DN PREV199900394228

TI Biology of marrow stromal cell lines derived from long-term bone marrow

cultures of Trp53-deficient mice.

AU Epperly, Michael W.; Bray, Jenifer A.; Carlos, Timothy M.; Prochownik,

Edward; Greenberger, Joel S. [Reprint author]

CS Departments of Radiation Oncology, Pediatrics and Medicine, University of

Pittsburgh Cancer Institute, 200 Lothrop Street, Pittsburgh, PA, 15213,

USA

SO Radiation Research, (July, 1999) Vol. 152, No. 1, pp. 29-40.

print.

CODEN: RAREAE. ISSN: 0033-7587.

DT Article

LA English

ED Entered STN: 28 Sep 1999

Last Updated on STN: 28 Sep 1999

AB To investigate the effect of Trp53 (formerly known as p53) on stromal

cells of the hematopoietic microenvironment, long-term bone marrow

cultures were established from mice in which the Trp53 gene had been

inactivated by homologous recombination (Trp53<sup>-/-</sup>) or their wild-type littermates (Trp53<sup>+/+</sup>). Long-term bone marrow cultures

from Trp53<sup>-/-</sup> mice continued to produce nonadherent cells for 22 weeks,

while Trp53<sup>+/+</sup> cultures ceased production after 15 weeks. There was a

significant increase in the number of nonadherent cells produced in

Trp53<sup>-/-</sup> long-term bone marrow cultures beginning at week 9 and continuing

to week 22 ( $P < 0.02$ ). The Trp53<sup>-/-</sup> cultures also showed significantly

increased cobblestone island formation indicative of early hematopoietic stem cell-containing colonies

beginning at week 10 ( $P < 0.01$ ). Cobblestone islands persisted until

weeks 15 and 22 in Trp53<sup>+/+</sup> and Trp53<sup>-/-</sup> cultures, respectively.

Co-cultivation experiments in which Trp53<sup>+/+</sup>Scal<sup>+</sup>lin<sup>-</sup> enriched hematopoietic stem cells were plated on Trp53<sup>-/-</sup> stromal cells showed

increased cobblestone island formation compared to Trp53<sup>-/-</sup> Scal<sup>+</sup>lin<sup>-</sup>

cells plated on Trp53<sup>+/+</sup> or Trp53<sup>-/-</sup> stromal cells. Radiation survival

curves for clonal bone marrow stromal cells revealed a similar D0 for the

Trp53<sup>+/+</sup> and Trp53<sup>-/-</sup> cell lines ( $1.62 \pm 0.16$  and  $1.49 \pm 0.08$  Gy,

respectively;  $P = 0.408$ ), and similar n ( $8.60 \pm 3.23$  and  $10.71 \pm 0.78$ ,

respectively) ( $P = 0.491$ ). Cell cycle analysis demonstrated a G2/M-phase

arrest that occurred 6 h after irradiation for both Trp53<sup>+/+</sup> and Trp53<sup>-/-</sup>

stromal cell lines. After 10 Gy irradiation, there was no significant

increase in the frequency of apoptosis detected in Trp53<sup>+/+</sup> compared to

Trp53<sup>-/-</sup> marrow stromal cell lines. In the stromal cell lines, ICAM-1 was

constitutively expressed on Trp53+/+ but not Trp53-/- cells; however, a 24-h exposure to TNF-alpha induced detectable ICAM-1 on Trp53-/- cells and increased expression on Trp53+/+ cells. To test the effect of Trp53 on the radiation biology of hematopoietic progenitor cells, the 32D cl 3 cell line was compared with a subclone in which expression of an E6 inserted transgene accelerates ubiquitin-dependent degradation of Trp53, thus preventing accumulation of Trp53 after genotoxic stress. The radiation survival curves were similar with no significant difference in the D0 or n, or in the percentage of cells undergoing apoptosis after 10 Gy irradiation between the two cell lines. Cells of the 32D-E6 cell line displayed a G2/M-phase arrest 6 h after 10 Gy, while cells of the parent line exhibited both a G2/M-phase arrest and a G1-phase arrest at 24 and 48 h. The results suggest a complex mechanism of action of Trp53 on the interactions between stromal and hematopoietic cells in long-term bone marrow cultures.

L21 ANSWER 8 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 1997:448965 BIOSIS

DN PREV199799748168

TI Murine embryonic stem cells without pig-a gene activity are competent for

hematopoiesis with the PNH phenotype but not for clonal expansion.

AU Rosti, Vittorio; Tremml, Gabi; Soares, Vera; Pandolfi, Pier Paolo;

Luzzatto, Lucio [Reprint author]; Bessler, Monica

CS Dep. Human Genetics, Memorial Sloan Kettering Cancer Cent., 1275 York

Ave., New York, NY 10021, USA

SO Journal of Clinical Investigation, (1997) Vol. 100, No. 5, pp. 1028-1036.

CODEN: JCINAO. ISSN: 0021-9738.

DT Article

LA English

ED Entered STN: 27 Oct 1997

Last Updated on STN: 27 Oct 1997

AB Paroxysmal nocturnal hemoglobinuria (PNH) develops in patients who have

had a somatic mutation in the X-linked PIG-A gene in a hematopoietic stem cell; as a result, a proportion of blood cells are deficient in all glycosyl phosphatidylinositol (GPI)-anchored proteins. Although the PIG-A mutation explains the phenotype of PNH cells, the mechanism enabling the PNH stem cell to expand is not clear. To examine this growth behavior, and to investigate the role of GPI-linked proteins in hematopoietic differentiation, we have inactivated the pig-a gene by homologous recombination in mouse embryonic stem (ES) cells. In mouse chimeras, pig-a- ES cells were able to contribute to hematopoiesis and to differentiate into mature red cells, granulocytes, and lymphocytes with the PNH phenotype. The proportion of PNH red cells was substantial in the fetus, but decreased rapidly after birth. Likewise, PNH granulocytes could only be demonstrated in the young mouse. In contrast, the percentage of lymphocytes deficient in GPI-linked proteins was more stable. In vitro, pig-a- ES cells were able to form pig-a-embryoid bodies and to undergo hematopoietic (erythroid and myeloid) differentiation. The number and the percentage of pig-a-embryoid bodies with hematopoietic differentiation, however, were significantly lower when compared with wild-type embryoid bodies. Our findings demonstrate that murine ES cells with a nonfunctional pig-a gene are competent for hematopoiesis, and give rise to blood cells with the PNH phenotype. pig-a inactivation on its own, however, does not confer a proliferative advantage to the hematopoietic stem cell. This provides direct evidence for the notion that some additional factor(s) are needed for the expansion of the mutant clone in patients with PNH.

L21 ANSWER 9 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 1996:432428 BIOSIS

DN PREV199699146034

TI Current experimental strategies for investigating human hematopoietic stem cell biology.

AU Ratajczak, Mariusz Z.; Gewirtz, Alan M.

CS Dep. Pathol., 515 Stellar-Chance Labs., 422 Curie Blvd., Univ. Pennsylvania Sch. Med., Philadelphia, PA 19104, USA

SO Folia Histochemica et Cytobiologica, (1996) Vol. 34, No. 2, pp.

59-67.

CODEN: FHCYEM. ISSN: 0239-8508.

DT Article

LA English

ED Entered STN: 26 Sep 1996

Last Updated on STN: 26 Sep 1996

AB The currently available different experimental strategies for investigating the biology of the human hematopoietic stem cells are

reviewed in this paper. There are discussed: (1) different approaches to isolate human hematopoietic stem cells, (2) available molecular techniques

for investigating gene expression in isolated cells, and (3) functional

tests evaluating their proliferative potential in in vitro cultures and in

vivo in animal models. Important information regarding stem cell biology

can be also gained from animal model involving: (1) overexpression of

particular genes in transgenic mice or, (2) gene "knock-out" techniques

using homologous recombination. The regulation of proliferation and differentiation of human hematopoietic stem cells can be

also discerned after downregulation of expression of genes of interest in

the early hematopoietic cells using antisense strategy.

L21 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2005:37226 CAPLUS

DN 142:174056

TI Erythropoietic porphyrias: Animal models and prospects for cellular and gene therapy in human

AU Ged, Cecile; Moreau-Gaudry, Francois; de Verneuil, Hubert

CS Laboratoire de Pathologie Moleculaire et Therapie Genique, Universite

Victor Segalen-Bordeaux II, Bordeaux, 33076, Fr.

SO Recent Research Developments in Human Genetics (2002), 1(Pt. 1), 253-271

CODEN: RRDHC6

PB Research Signpost

DT Journal; General Review

LA English

AB A review. Recent progress in mol. technol. has resulted in precise

knowledge of the genes involved in the heme biosynthetic pathway as well

as rapid development of innovative tools including animal models and gene

transfer strategies aimed at a better understanding of pathogenesis and treatment of porphyrias. Animal models of erythropoietic porphyrias occur naturally, are obtained by chemical mutagenesis, or created by homologous recombination in transgenic mice. Successful gene transfer expts. performed both in vitro, in hematopoietic progenitor cells, and in vivo demonstrate the feasibility of somatic gene therapy in erythropoietic porphyrias. Sufficient gene transfer rate, and convenient metabolic correction in disease cells, as well. As phenotypic reversion when a mouse model was available, have been documented in protoporphyria (ferrochelatase deficiency) and congenital erythropoietic porphyria (uroporphyrinogen III synthase deficiency). This confirms that erythropoietic porphyrias are good candidates for the treatment of hematopoietic stem cells by gene therapy.

RE.CNT 129 THERE ARE 129 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1994:601809 CAPLUS

DN 121:201809

OREF 121:36667a,36670a

TI The hematopoietic cell-specific gene D4 and its use in the study of

hematopoiesis

IN Lim, Bing; Lelias, Jean-Michel; Adra, Chaker N.; Ko, Jone L.

PA Cytomed, Inc., USA; Beth Israel Hospital Association

SO PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

DATE	PATENT NO.	KIND	DATE	APPLICATION NO.
19931210 <--	WO 9413802	A1	19940623	WO 1993-US12074
	W: AU, CA, JP			
PT, SE	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL,			
19931210 <--	AU 9457486	A	19940704	AU 1994-57486
	US 5767073	A	19980616	US 1994-252073
19940601 <--				

US 5585478                      A            19961217            US 1994-292945  
 19940818 <--  
 PRAI US 1992-990337            A            19921210  
       WO 1993-US12074            W            19931210  
 AB    A cDNA clone, denoted D4, of human or mouse that is  
 preferentially  
       expressed in hematopoietic cells is cloned and expressed for use  
 in the  
       study of the function of the protein. The human cDNA clone has  
 been  
       expressed in bacteria and the predicted 24 Kd protein purified  
 and cDNA  
       was used to obtain several full length mouse genomic clones.  
 Sequence  
       comparisons indicate that D4 is similar to the bovine rhoGDI  
 protein and  
       so may function as a GDP-dissociation inhibitor of at least  
 several small  
       GTP-binding proteins (CDC42 and rac). The D4 protein was used  
 to generate  
       a polyclonal antibody sp. for the protein. A clone has been  
 analyzed and  
       sequenced to use for the construction of a gene-targeting vector  
 to  
       produce animals deficient in D4 through disruption of the gene by  
 homologous recombination. These animals can then be  
 used as models for fundamental and applied research on the  
 GTP-binding  
       proteins. Hematopoietic cell-specific cDNAs were cloned using  
 subtractive  
       libraries from hematopoietic stem cell lines  
 as probes for a cDNA library from K562 cells. Patterns of  
 transcription  
       of the gene in differentiating human cell lines in culture and in  
 developing mouse were determined and the restriction of  
 expression to  
       hematopoietic cells demonstrated although it may not be relevant  
 to  
       erythropoiesis or embryonic hematopoiesis.

L21 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN  
 AN 1993:139047 CAPLUS  
 DN 118:139047  
 OREF 118:23706h,23707a  
 TI Targeted gene modification for gene therapy of stem cells  
 AU Boggs, Sallie S.; Bahnson, Alfred B.  
 CS Sch. Med., Univ. Pittsburgh, Pittsburgh, PA, USA  
 SO Concise Rev. Clin. Exp. Hematol. (1992), 319-30. Editor(s):  
       Murphy, Martin J., Jr. Publisher: AlphaMed, Dayton, Ohio.  
       CODEN: 58NOAO  
 DT Conference; General Review  
 LA English

AB A review with 117 refs. Ideally, gene therapy would correct the specific

gene defect without adding potentially harmful extraneous DNA sequences.

Such correction can be obtained by homologous recombination (HR) between newly added DNA sequences and identical

(homologous) sequences in the genomic target. Hematopoietic stem cells

(HSC) are the necessary targets for gene therapy of hemoglobinopathies.

Unfortunately, the low efficiency of HR and the fact that HSC are rare,

noncycling cells that are difficult to expand in culture makes HR in HSC

impractical. However, technol. developments in HSC purification, culture, and

assay, increasing knowledge of factors affecting HR efficiency, and

powerful new selection systems are increasing the likelihood of using HR

in HSC. Meanwhile, the ability of adeno-associated virus (AAV) to target a

specific chromosome site in nondividing cells makes AAV vectors attractive

for gene therapy with HSC. Alternately, embryo stem (ES) cells with genes

modified by HR might be made to differentiate to HSC. These advances are

reviewed with particular emphasis on approaches to targeted gene modification of HSC and speculation on directions for future

research.

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reserved on STN

AN 2002352842 EMBASE

TI Lack of neighborhood effects from a transcriptionally active phosphoglycerate kinase-neo cassette located between the murine  $\beta$ -major and  $\beta$ -minor globin genes.

AU Kaufman, Richard M.; Lu, Zhi Hong; Behl, Rajesh; Holt, Jo M.; Ackers, Gary

K.; Ley, Timothy J. (correspondence)

CS Division of Oncology, Section of Stem Cell Biology, Washington Univ.

School of Medicine, 660 South Euclid Ave, St Louis, MO 63110-1093, United

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SO Blood, (1 Jul 2001) Vol. 98, No. 1, pp. 65-73.

Refs: 42

ISSN: 0006-4971 CODEN: BLOOAW

CY United States



DT Journal; Article  
FS 025 Hematology  
LA English  
SL English  
ED Entered STN: 31 Oct 2002  
Last Updated on STN: 31 Oct 2002  
AB For the treatment of  $\beta$ -globin gene defects, a homologous recombination-mediated gene correction approach would provide advantages over random integration-based gene therapy strategies. However, "neighborhood effects" from retained selectable marker genes in the targeted locus are among the key issues that must be taken into consideration for any attempt to use this strategy for gene correction.  
An Ala-to-Ile mutation was created in the  $\beta 6$  position of the mouse  $\beta$ -major globin gene ( $\beta(61)$ ) as a step toward the development of a murine model system that could serve as a platform for therapeutic gene correction studies. The marked  $\beta$ -major gene can be tracked at the level of DNA, RNA, and protein, allowing investigation of the impact of a retained phosphoglycerate kinase (PGK)-neo cassette located between the mutant  $\beta$ -major and  $\beta$ -minor globin genes on expression of these 2 neighboring genes. Although the PGK-neo cassette was expressed at high levels in adult erythroid cells, the abundance of the  $\beta(61)$  mRNA was indistinguishable from that of the wildtype counterpart in bone marrow cells. Similarly, the output from the  $\beta$ -minor globin gene was also normal. Therefore, in this specific location, the retained, transcriptionally active PGK-neo cassette does not disrupt the regulated expression of the adult  $\beta$ -globin genes. .COPYRGT. 2001 by The American Society of Hematology.

L21 ANSWER 14 OF 24 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

AN 2000433831 EMBASE

TI Gene correction in hematopoietic progenitor cells by homologous recombination.

AU Hatada, Seigo; Bentley, Stuart A.; Smithies, Oliver (correspondence)

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University of North Carolina, Chapel Hill, NC 27599-7525, United States.

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AU Nikkuni, Koji

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AU Smithies, Oliver (correspondence)

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SO Proceedings of the National Academy of Sciences of the United  
States of

America, (5 Dec 2000) Vol. 97, No. 25, pp. 13807-13811.

Refs: 24

ISSN: 0027-8424 CODEN: PNASA6

CY United States

DT Journal; Article

FS 022 Human Genetics

025 Hematology

029 Clinical and Experimental Biochemistry

LA English

SL English

ED Entered STN: 29 Dec 2000

Last Updated on STN: 29 Dec 2000

AB Homologous recombination (gene targeting) has many  
desirable features for gene therapy, because it can precisely  
correct

mutant genes and restore their normal expression, and random  
nonhomologous

integration of DNA is infrequent in cells in which homologous  
recombination has occurred. There are, however, no reports of  
attempts to use homologous recombination to correct

mutant genes in normal hematopoietic stem cells (HSCs), which  
are prime

cells for therapy of a variety of hematological and other  
conditions,

presumably because of their low abundance and uncertainty that  
homologous recombination can occur at a usable frequency  
in these cells. The experiments reported here encourage

optimism in this

respect by demonstrating targeted correction of a defective  
hypoxanthine

phosphoribosyltransferase gene in hematopoietic progenitor cells  
that can

form colonies in methylcellulose culture. These clonogenic  
cells are in

the same lineage as HSCs but are more abundant and more mature  
and so less

pluripotent. Corrected colonies were identified by their survival in selective medium after electroporation of correcting DNA into unfractionated mouse bone marrow cells and were confirmed by reverse transcription-PCR and sequencing. The observed frequency ( $4.4 \pm 3.3 \times 10^{-5}$ ) per treated clonogenic cell) is the same as in embryonic stem cells ( $2.3 \pm 0.4 \times 10^{-5}$ ) with the same DNA and mutation. These data suggest that gene targeting to correct mutant genes eventually will prove feasible in HSCs capable of long-term bone marrow reconstitution.

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AN 2000303186 EMBASE

TI Thrombasthenic mice generated by replacement of the integrin  $\alpha$ (IIb)

gene: Demonstration that transcriptional activation of this megakaryocytic

locus precedes lineage commitment.

AU Tronik-Le Roux, D. (correspondence); Roullot, V.; Poujol, C.; Kortulewski,

T.; Nurden, P.; Marguerie, G.

CS Commissariat a l'Energie Atomique, Dept. de Radiobiol. et Radiopathol.,

CEA-Evry, 2 rue Gaston Cremieux, 91057 Evry Cedex, France. leroux@dsvidf.c

ea.fr

SO Blood, (15 Aug 2000) Vol. 96, No. 4, pp. 1399-1408.

Refs: 60

ISSN: 0006-4971 CODEN: BLOOAW

CY United States

DT Journal; Article

FS 025 Hematology

029 Clinical and Experimental Biochemistry

LA English

SL English

ED Entered STN: 21 Sep 2000

Last Updated on STN: 21 Sep 2000

AB To analyze the transcriptional activity of the gene encoding the  $\alpha$

subunit of the platelet integrin  $\alpha$ (IIb) $\beta$ (3) during the hematopoietic differentiation, mice were produced in which the herpes

virus thymidine kinase (tk) was introduced in this megakaryocytic specific

locus using homologous recombination technology. This

provided a convenient manner in which to induce the eradication

of

particular hematopoietic cells expressing the targeted gene. Results of progenitor cell cultures and long-term bone marrow (BM) assays showed that the growth of a subset of stem cells was reduced in the presence of the antiherpetic drug ganci-clovir, demonstrating that the activation of the toxic gene occurs before the commitment to the megakaryocytic lineage. Furthermore the knock-in of the tk gene into the  $\alpha$ (IIb) locus resulted in the knock-out of the  $\alpha$ (IIb) gene in homozygous mice. Cultures of BM cells of these animals, combined with ultrastructural analysis, established that the  $\alpha$ (IIb) glycoprotein is dispensable for lineage commitment and megakaryocytic maturation. Platelets collected from  $\alpha$ (IIb)-deficient mice failed to bind fibrinogen, to aggregate, and to retract a fibrin clot. Moreover, platelet  $\alpha$ -granules did not contain fibrinogen. Consistent with these characteristics, the mice displayed bleeding disorders similar to those in humans with Glanzmann thrombasthenia. (C) 2000 by The American Society of Hematology.

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reserved on STN

AN 2000255733 EMBASE

TI Insertion of enhanced green fluorescent protein into the lysozyme gene

creates mice with green fluorescent granulocytes and macrophages.

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10461, United States. graf@aeacom.yu.edu

AU Faust, Nicole; Varas, Florencio; Kelly, Louise M.; Heck, Susanne

SO Blood, (15 Jul 2000) Vol. 96, No. 2, pp. 719-726.

Refs: 20

ISSN: 0006-4971 CODEN: BLOOAW

CY United States

DT Journal; Article

FS 025 Hematology

LA English

SL English

ED Entered STN: 10 Aug 2000

Last Updated on STN: 10 Aug 2000

AB Pluripotent hematopoietic stem cells have been studied extensively, but

the events that occur during their differentiation remain largely uncharted. To develop a system that allows the differentiation of cultured multipotent progenitors by time-lapse fluorescence microscopy, myelomonocytic cells were labeled with green fluorescent protein (GFP) in vivo. This was achieved by knocking the enhanced GFP (EGFP) gene into the murine lysozyme M (lys) locus and using a targeting vector, which contains a neomycin resistant (neo) gene flanked by LoxP sites and 'splinked' ends, to increase the frequency of homologous recombination. Analysis of the blood and bone marrow of the lys- EGFP mice revealed that most myelomonocytic cells, especially mature neutrophil granulocytes, were fluorescence-positive, while cells from other lineages were not. Removal of the neo gene through breeding of the mice with the Cre-deleter strain led to an increased fluorescence intensity. Mice with an inactivation of both copies of the lys gene developed normally and were fertile.

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by The American Society of Hematology.

L21 ANSWER 17 OF 24 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights

reserved on STN  
AN 1999344567 EMBASE  
TI Preferential liver irradiation enhances hematopoiesis through a thrombopoietin-independent mechanism.  
AU Mouthon, Marc-Andre (correspondence); Vandamme, Marie; Gourmelon, Patrick  
CS Inst. de Protect. et de Surete Nucl., IPSN B.P. no. 6, F-92265 Fontenay-aux-Roses Cedex, France.  
AU Vainchenker, William; Wendling, Francoise  
CS INSERM U362, Institut Gustave Roussy, F-94805, Villejuif Cedex, France.  
AU Mouthon, Marc-Andre (correspondence)  
CS Institut Protection/Surete Nucleaire, IPSN B.P. no. 6, F-92265 Fontenay-aux-Roses Cedex, France.  
SO Radiation Research, (Oct 1999) Vol. 152, No. 4, pp. 390-397.  
Refs: 45  
ISSN: 0033-7587 CODEN: RAREAE  
CY United States  
DT Journal; Article  
FS 025 Hematology  
046 Environmental Health and Pollution Control  
048 Gastroenterology

LA English  
 SL English  
 ED Entered STN: 21 Oct 1999  
 Last Updated on STN: 21 Oct 1999  
 AB Liver synthesizes thrombopoietin, which is a major cytokine involved in the production of hematopoietic cells. The purpose of this study was to examine the effects of preferential liver irradiation on expression of thrombopoietin and production of hematopoietic cells. About 70% of the liver of C57BL6/J mice was irradiated with 20 Gy of  $\gamma$  rays. Exposure to ionizing radiation enhanced hematopoietic progenitors and megakaryocyte frequency in bone marrow and induced a transient increase in platelet and neutrophil counts that peaked 14 days after irradiation. The concentration of thrombopoietin was increased in serum as early as 5 h after liver irradiation and was still elevated at day 14. By using Northern blot analysis and an RNase protection assay, we showed that thrombopoietin mRNA was increased in the irradiated liver. To determine whether thrombopoietin was involved in the stimulation of hematopoiesis, we irradiated mice in which thrombopoietin deficiency had been induced by homologous recombination. Platelet levels were increased in both heterozygous and homozygous thrombopoietin-deficient mice with a magnitude similar to that obtained in normal mice. In summary, our data demonstrate that local irradiation of the abdomen encompassing the liver leads to stimulation of hematopoiesis through a thrombopoietin-independent mechanism.

L21 ANSWER 18 OF 24 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN  
 AN 1999201541 EMBASE  
 TI Expression of the transcription factor GATA-3 is required for the development of the earliest T cell progenitors and correlates with stages of cellular proliferation in the thymus.  
 AU Hendriks, Rudolf W. (correspondence); Van Doorninck, Hikke; Grosveld,

Frank; Karis, Alar  
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 hendriks@immu.fgg.eur.nl;  
 hendricks@immu.fgg.eur.nl  
 AU Hendriks, Rudolf W. (correspondence); Nawijn, Martijn C.  
 CS Department of Immunology, Faculty of Medicine, Erasmus University  
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 hendriks@immu.fgg.eur.nl; hendricks@immu.fgg.eur.nl  
 AU Engel, J. Douglas  
 CS Department of Biochemistry, Molecular Biology and Cell Biology,  
 Northwestern University, Evanston, IL, United States.  
 AU Karis, Alar  
 CS Inst. of Molecular and Cell Biology, University of Tartu, 23  
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 51010 Tartu, Estonia.  
 SO European Journal of Immunology, (1999) Vol. 29, No. 6, pp.  
 1912-1918.  
 Refs: 24  
 ISSN: 0014-2980 CODEN: EJIMAF  
 CY Germany  
 DT Journal; Article  
 FS 021 Developmental Biology and Teratology  
 026 Immunology, Serology and Transplantation  
 029 Clinical and Experimental Biochemistry  
 LA English  
 SL English  
 ED Entered STN: 1 Jul 1999  
 Last Updated on STN: 1 Jul 1999  
 AB GATA-3 is a zinc-finger transcription factor that is essential  
 for both  
 early T cell development and Th2 cell differentiation. To  
 quantify GATA-3  
 expression during T cell development in vivo in the mouse, the  
 GATA-3 gene  
 was targeted by insertion of a lacZ reporter by homologous  
 recombination in embryonic stem (ES) cells. Although we could  
 detect GATA-3(+) cells throughout T cell development in the  
 thymus, the  
 proportions of GATA-3(+) cells varied considerably between the  
 distinct  
 differentiation stages. The two periods of TCR  $\alpha$  and  $\beta$  gene  
 recombination, which occur in quiescent or slowly dividing  
 cells, were  
 associated with low proportions of GATA-3(+) cells. Conversely,  
 the stage  
 of rapidly proliferating cells, which insulates these two waves  
 of TCR  
 rearrangement, was characterized by a large proportion of  
 GATA-3(+) cells.  
 In addition, we generated chimeric mice by injection of  
 GATA-3-deficient

lacZ-expressing ES cells into wild-type blastocysts. In this in vivo competition analysis, no contribution of GATA-3-deficient cells to the T cell lineage was detected, not even in the earliest CD44(+)CD25(-) double-negative (CD4(-)CD8(-)) cell stage in the thymus. These results parallel data implicating other GATA family members as key regulators of proliferation and survival of early hematopoietic cells. We therefore propose that GATA-3 is required for the expansion of T cell progenitors, and for the control of subsequent proliferation steps, which alternate periods of TCR recombination in the thymus.

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AN 1999046991 EMBASE

TI Permissive role of thrombopoietin and granulocyte colony-stimulating

factor receptors in hematopoietic cell fate decisions in vivo.

AU Stoffel, Ruedi; Ziegler, Sandra; Ghilardi, Nico; Skoda, Radek C. (correspondence)

CS Biozentrum, University of Basel, Klingelbergstrasse 70, 4056 Basel, Switzerland. skoda@ubaclu.unibas.ch

AU Ledermann, Birgit

CS Novartis Inc., P.O. Box, 4001 Basel, Switzerland.

AU De Sauvage, Frederic J.

CS Genentech Inc., Department of Oncology, 460 Point San Bruno Boulevard, South San Francisco, CA 94080, United States.

SO Proceedings of the National Academy of Sciences of the United States of

America, (19 Jan 1999) Vol. 96, No. 2, pp. 698-702.

Refs: 34

ISSN: 0027-8424 CODEN: PNASA6

CY United States

DT Journal; Article

FS 021 Developmental Biology and Teratology  
025 Hematology

LA English

SL English

ED Entered STN: 25 Feb 1999

Last Updated on STN: 25 Feb 1999

AB The question of whether extracellular signals influence hematopoiesis by

instructing stem cells to commit to a specific hematopoietic lineage



(instructive model) or solely by permitting the survival and proliferation of predetermined progenitors (permissive model) has been controversial since the discovery of lineage-dominant hematopoietic cytokines. To study the potential role of cytokines and their receptors in hematopoietic cell fate decisions, we used homologous recombination to replace the thrombopoietin receptor gene (mpl) with a chimeric construct encoding the extracellular domain of mpl and the cytoplasmic domain of the granulocyte colony-stimulating factor receptor (G-CSFR). This chimeric receptor binds thrombopoietin but signals through the G-CSFR intracellular domain. We found that, despite the absence of a functional mpl signaling domain, homozygous knock-in mice had a normal platelet count, indicating that in vivo the cytoplasmic domain of G-CSFR can functionally replace mpl signaling to support normal megakaryopoiesis and platelet formation. This finding is compatible with the permissive model, according to which cytokine receptors provide a nonspecific survival or proliferation signal, and argues against an instructive role of mpl or G-CSFR in hematopoietic cell fate decisions.

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AN 1997351557 EMBASE

TI [New concepts on osteoclast origin: Relationship with normal and inflammatory macrophages].

Nouveaux concepts sur l'origine des osteoclastes: Relation avec les macrophages normaux et inflammatoires.

AU Solari, Florence (correspondence); Jurdic, Pierre

CS Lab. de Biol. Molec. et Cellulaire, UMR 49 Cnrs/Ens, Ecl. Normale Sup. de

Lyon, 46, allée d'Italie, 69364 Lyon Cedex 07, France.

AU Solari, Florence (correspondence)

CS Lab biologie moleculaire cellulaire, UMR 49 Cnrs-Ens, equipe Inra 913,

Ecole normale superieure de Lyon, 46 allée d'Italie, 69364 Lyon Cedex 07, France.

SO Medecine/Sciences, (Nov 1997) Vol. 13, No. 11, pp. 1285-1293.  
 Refs: 47  
 ISSN: 0767-0974 CODEN: MSMSE4  
 CY France  
 DT Journal; General Review; (Review)  
 FS 025 Hematology  
 029 Clinical and Experimental Biochemistry  
 033 Orthopedic Surgery  
 LA French  
 SL French; English  
 ED Entered STN: 4 Dec 1997  
 Last Updated on STN: 4 Dec 1997  
 AB Osteoclasts are bone resorbing multinucleated giant cells. They  
 derive  
 from the fusion of hemopoietic mononucleated precursor cells,  
 although  
 their precise origin along the hemopoietic differentiation  
 pathway is  
 still a matter of discussion. Recent data obtained both in vivo  
 and in  
 vitro sustain the idea that osteoclasts derive from fusion of  
 cells at the  
 late stages of the monocytic pathway, or even directly from  
 macrophages.  
 Osteoclasts, as well as macrophages, are phagocytic cells  
 sharing in  
 common many surface antigens. In vitro models have been  
 developped  
 enabling formation of osteoclasts directly from resident tissue  
 microphages. Furthermore, analysis of osteopetrotic mice,  
 obtained from  
 either spontaneous mutations or after homologous  
 recombinations, have shown that macrophages and osteoclasts are  
 closely related. Finally, osteoclasts appear also to be highly  
 related to  
 polycaryonic macrophages found in inflammatory tissues. Here,  
 we propose  
 that only one way of differentiation leads from  
 monocytes/macrophages to  
 either inflammatory macrophages or bone resorbing osteoclasts,  
 the final  
 commitment depending upon microenvironment conditions.

L21 ANSWER 21 OF 24 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All  
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 AN 1997282875 EMBASE  
 TI A BCR-ABL(p190) fusion gene made by homologous  
 recombination causes B- cell acute lymphoblastic leukemias in  
 chimeric mice with independence of the endogenous bcr product.  
 AU Sanchez-Garcia, I., Dr. (correspondence)  
 CS Depto. Proliferacion y D., Inst. de Microbiol. Bioquim., Edificio

Departamental, Avda del Campo Charro s/n, 37007-Salamanca, Spain.

AU Castellanos, A.; Pintado, B.; Weruaga, E.; Arevalo, R.; Lopez, A.; Orfao, A.

AU Sanchez-Garcia, I., Dr. (correspondence)

CS DPDC, Inst. de Microbiologia Bioquimica, Edificio Departamental, Avda del Campo Charro s/n, 37007-Salamanca, Spain.

SO Blood, (15 Sep 1997) Vol. 90, No. 6, pp. 2168-2174.

Refs: 43

ISSN: 0006-4971 CODEN: BLOOAW

CY United States

DT Journal; Article

FS 016 Cancer

022 Human Genetics

025 Hematology

LA English

SL English

ED Entered STN: 16 Oct 1997

Last Updated on STN: 16 Oct 1997

AB BCR-ABL(p190) oncogene is the result of a reciprocal translocation between

chromosomes g and 22 and is associated with B-cell acute lymphoblastic

leukemia (B-ALL) in humans. Current models expressing the BCR-ABL(p190)

chimeric gene fail to consistently reproduce the phenotype with which the

fusion gene is associated in human pathology, mainly due to the difficulty

of being expressed in the appropriate cell type in vivo. We have used

here homologous recombination in ES cells to create an

in-frame fusion of BCR-ABL(p190)that mimics the consequences of the human

chromosomal translocation by fusion of BCR-ABL coding sequences into the

bcr endogenous gene. The chimeric mice generated with the mutant embryonic stem cells systematically develop B-ALL. Using these chimeric

mice, we further show that BCR-ABL oncogene does not require the endogenous bcr product in leukemogenesis. Our results show that BCR-ABL(p190) chimeric mice are a new model to study the biology of the

BCR-ABL oncogene and indicate the efficacy of this strategy for studying

the role of specific chromosome abnormalities in tumor development.

reserved on STN

AN 1997200596 EMBASE

TI A 'knockdown' mutation created by cis-element gene targeting reveals the dependence of erythroid cell maturation on the level of transcription factor GATA-1.

AU McDevitt, M.A.; Shivdasani, R.A.; Fujiwara, Y.; Yang, H.; Orkin, S.H.

(correspondence)

CS Division of Hematology/Oncology, Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, United States. orkin@rascal.med.harvard.edu

SO Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 13, pp. 6781-6785.

Refs: 32

ISSN: 0027-8424 CODEN: PNASA6

CY United States

DT Journal; Article

FS 001 Anatomy, Anthropology, Embryology and Histology  
 021 Developmental Biology and Teratology  
 025 Hematology  
 029 Clinical and Experimental Biochemistry

LA English

SL English

ED Entered STN: 31 Jul 1997  
 Last Updated on STN: 31 Jul 1997

AB The hematopoietic-restricted transcription factor GATA-1 is required for both mammalian erythroid cell and megakaryocyte differentiation. To define the mechanisms governing its transcriptional regulation, we replaced upstream sequences including a DNase 1 hypersensitive (HS) region with a neomycin- resistance cassette by homologous recombination in mouse embryonic stem cells and generated mice either harboring this mutation (neo $\Delta$ HS) or lacking the selection cassette ( $\Delta$ neo $\Delta$ HS). Studies of the consequences of these targeted mutations provide novel insights into GATA-1 function in erythroid cells. First, the neo $\Delta$ HS mutation leads to a marked impairment in the rate or efficiency of erythroid cell maturation due to a modest (4- to 5-fold) decrease in GATA-1 expression. Hence, erythroid differentiation is dose- dependent with respect to GATA-1. Second, since expression of GATA-1 from the  $\Delta$ neo $\Delta$ HS allele in erythroid cells is largely restored, transcription interference imposed by the introduced cassette must account for the 'knockdown' effect of the

mutation. Finally, despite the potency of the upstream sequences in conferring high-level, developmentally appropriate expression of transgenes in mice, other cis-regulatory elements within the GATA-1 compensate for its absence in erythroid cells. Our work illustrates the usefulness of targeted mutations to create knockdown mutations that may uncover important quantitative contribution of gene function not revealed by conventional knockouts.

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AN 1996134420 EMBASE

TI CD34-deficient mice have reduced eosinophil accumulation after allergen

exposure and show a novel crossreactive 90-kD protein.

AU Suzuki, Akira, Dr. (correspondence)

CS Ontario Cancer Institute, Depts. of Med. Biophys. and Immunol., University

of Toronto, 620 University Ave, Toronto, Ont. M5G 2C1, Canada.

AU Andrew, David P.; Gonzalo, Jose-Angel; Fukumoto, Manabu; Spellberg, Jason;

Hashiyama, Motohiro; Takimoto, Hiroaki; Gerwin, Nicole; Webb, Lain;

Molineux, Graham; Amakawa, Ryuichi; Tada, Yoshifumi; Wakeham, Andrew;

Brown, John; McNiece, Ian; Ley, Klaus; Butcher, Eugene C.; Suda, Toshio;

Gutierrez-Ramos, Jose-Carlos; Mak, Tak Wah

AU Suzuki, Akira, Dr. (correspondence)

CS Amgen Institute, Ontario Cancer Institute, University of Toronto, 620

University Ave, Toronto, Ont. M5G 2C1, Canada.

SO Blood, (1 May 1996) Vol. 87, No. 9, pp. 3550-3562.

Refs: 58

ISSN: 0006-4971 CODEN: BLOOAW

CY United States

DT Journal; Article

FS 026 Immunology, Serology and Transplantation

LA English

SL English

ED Entered STN: 20 May 1996

Last Updated on STN: 20 May 1996

AB CD34 is expressed on the surface of hematopoietic stem/progenitor cells,

stromal cells, and on the surface of high-endothelial venules (HEV). CD34

binds L-selectin, an adhesion molecule important for leukocyte rolling on

venules and lymphocyte homing to peripheral lymph nodes (PLN).  
 We generated CD34-deficient mutant animals through the use of  
 homologous recombination. Wild-type and mutant animals  
 showed no differences in lymphocyte binding to PLN HEV, in  
 leukocyte rolling on venules or homing to PLN, in neutrophil extravasation  
 into peritoneum in response to inflammatory stimulus, nor in delayed  
 type hypersensitivity. Anti-L-selectin monoclonal antibody (MEL-14)  
 also inhibited these immune responses similarly in both  
 CD34-deficient and wild-type mice. However, eosinophil accumulation in the lung  
 after inhalation of a model allergen, ovalbumin, is several-fold lower  
 in mutant mice. We found no abnormalities in hematopoiesis in adult mice  
 and interactions between mutant progenitor cells and a stromal cell  
 line in vitro were normal. No differences existed in the recovery of  
 progenitor cells after 5- fluorouracil treatment, nor in the mobilization of  
 progenitor cells after granulocyte colony-stimulating factor  
 treatment compared with wild-type animals. Surprisingly, although CD34  
 was not expressed in these mice, a portion of its 90-kD band  
 crossreactive with MECA79 remained after Western blot. Thus, we have identified an  
 additional molecule(s) that might be involved in leukocyte  
 trafficking. These results indicate that CD34 plays an important role in  
 eosinophil trafficking into the lung.

L21 ANSWER 24 OF 24 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All  
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AN 1995209723 EMBASE

TI Failure of blood-island formation and vasculogenesis in Flk-1  
 deficient mice.

AU Shalaby, F.; Rossant, J. (correspondence); Yamaguchi, T.P.;  
 Gertsenstein,

M.; Wu, X.-F.; Breitman, M.L.; Schuh, A.C.

CS Samuel Lunenfeld Research Institute, Mount Sinai Hospital, 600  
 University

Avenue, Toronto, Ont. M5G 1X5, Canada.

SO Nature, (1995) Vol. 376, No. 6535, pp. 62-66.

ISSN: 0028-0836 CODEN: NATUAS

CY United Kingdom

DT Journal; Article

FS 001 Anatomy, Anthropology, Embryology and Histology

021 Developmental Biology and Teratology

025 Hematology

LA English

SL English

ED Entered STN: 3 Aug 1995

Last Updated on STN: 3 Aug 1995

AB The receptor tyrosine kinase Flk-1 is believed to play a pivotal role in

endothelial development. Expression of the Flk-1 receptor is restricted

to endothelial cells and their embryonic precursors, and is complementary

to that of its ligand, vascular endothelial growth factor (VEGF), which is

an endothelial-specific mitogen. Highest levels of flk-1 expression are

observed during embryonic vasculogenesis and angiogenesis, and during

pathological processes associated with neovascularization, such as tumour

angiogenesis. Because flk-1 expression can be detected in presumptive

mesodermal yolk-sac blood-island progenitors as early as 7.0 days postcoitum, Flk-1 may mark the putative common embryonic

endothelial and

haematopoietic precursor, the haemangioblast, and thus may also be

involved in early haematopoiesis. Here we report the generation of mice

deficient in Flk-1 by disruption of the gene using homologous recombination in embryonic stem (ES) cells. Embryos homozygous for this mutation die in utero between 8.5 and 9.5 days

post-coitum, as a

result of an early defect in the development of haematopoietic and

endothelial cells. Yolk-sac blood islands were absent at 7.5 days,

organized blood vessels could not lie observed in the embryo or yolk sac

at any stage, and haematopoietic progenitors were severely reduced. These

results indicate that Flk-1 is essential for yolk-sac blood-island

formation and vasculogenesis in the mouse embryo.

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	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	
-5.74		

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NEWS 5 FEB 02 Simultaneous left and right truncation (SLART) added  
for CERAB, COMPUAB, ELCOM, and SOLIDSTATE  
NEWS 6 FEB 02 GENBANK enhanced with SET PLURALS and SET SPELLING  
NEWS 7 FEB 06 Patent sequence location (PSL) data added to USGENE  
NEWS 8 FEB 10 COMPENDEX reloaded and enhanced  
NEWS 9 FEB 11 WTEXTILES reloaded and enhanced  
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NEWS 13 FEB 23 MEDLINE now offers more precise author group fields  
and 2009 MeSH terms  
NEWS 14 FEB 23 TOXCENTER updates mirror those of MEDLINE - more  
precise author group fields and 2009 MeSH terms  
NEWS 15 FEB 23 Three million new patent records blast AEROSPACE  
into  
STN patent clusters  
NEWS 16 FEB 25 USGENE enhanced with patent family and legal status  
display data from INPADOCDB  
NEWS 17 MAR 06 INPADOCDB and INPAFAMDB enhanced with new display  
formats  
NEWS 18 MAR 11 EPFULL backfile enhanced with additional full-text  
applications and grants  
NEWS 19 MAR 11 ESBIOBASE reloaded and enhanced  
NEWS 20 MAR 20 CAS databases on STN enhanced with new super role  
for nanomaterial substances  
NEWS 21 MAR 23 CA/CAPLUS enhanced with more than 250,000 patent  
equivalents from China  
NEWS 22 MAR 30 IMSPATENTS reloaded and enhanced  
NEWS 23 APR 03 CAS coverage of exemplified prophetic substances  
enhanced  
NEWS 24 APR 07 STN is raising the limits on saved answers  
  
NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,  
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.  
  
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FILE 'EMBASE' ENTERED AT 14:59:20 ON 20 APR 2009  
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=> s multipotent adult stem cell or MAPC  
L1            348 MULTIPOTENT ADULT STEM CELL OR MAPC

=> s l1 and homologous recombina?  
L2            3 L1 AND HOMOLOGOUS RECOMBIN?

=> dup rem l2  
PROCESSING COMPLETED FOR L2  
L3            2 DUP REM L2 (1 DUPLICATE REMOVED)

=> d bib abs 1-y  
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"DISPLAY HISTORY" to locate the file the L# was created in, use the  
FILE command to enter that file, and re-enter the DISPLAY ACC  
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L3 ANSWER 1 OF 2 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

DUPLICATE 1

AN 2008:88063 BIOSIS

DN PREV200800088197

TI Stem cells and embryonic stem cells: Biological differences.  
Original Title: Celulas madre y celulas troncoembrionarias:  
Diferencias biologicas.

AU Riveros, Dolly Macias [Reprint Author]; Vazquez Chagoyan, Juan Carlos;

Morales, Rogelio Alonso; Juarez, Marco Cajero

CS Univ Autonoma Estado Mexico, Fac Med Vet and Zootecnia, Program Estudios

Avanzados Salud Anim, Km 15 5, Mexico City, DF, Mexico  
marmac4@uaemex.mx; jcvvc@uaemex.mx; ralonsom@servidor.unam.mx;  
cajeromarco@hotmail.com

SO Veterinaria Mexico, (OCT-DEC 2007) Vol. 38, No. 4, pp. 477-501.  
CODEN: VTERBU. ISSN: 0301-5092.

DT Article

LA Spanish

ED Entered STN: 23 Jan 2008

Last Updated on STN: 23 Jan 2008

AB The stem cells have been classified in three types according to their

natural niche of origin, aptitude and differential function: totipotential,

pluripotential and multipotential; the first, called embryonic stem cells

(ES) originate from the morulae; the second, come from the inner cell mass

of the blastocyst (ICM); and the third, known as multipotent adult

progenitor cells (MAPC) are found in some adult tissues. The biological difference lies in their capabilities to produce cell lines,

the totipotentials have the faculty to originate a complete organism, the

pluripotential can generate all the cellular types and even the germinal

line and the multipotentials can derivate in specific lineages. The stem

cells are able to self-renew, and originate daughter-cells compromised

with certain development routes; they are characterized for their indefinite division and are morphologically and functionally differentiated. When the stem cells and some progenitor types

are

extracted from their natural environment and are grown in vitro, in

suitable medium, can be transfected and remain in an undifferentiated state without losing their potentiality; thus, when they are reintegrated to blastocyst receptors they are able to go on with their development.

The study and compilation of information about these biological qualities of differential function, as well as their usefulness in homologous recombination and production of animal models that generate recombinant proteins, applicable for preventive-regenerating medicine and treatment of diseases, constitute the aim of this work.

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2004:493864 CAPLUS

DN 141:66248

TI Homologous recombination in multipotent adult progenitor cells

IN Verfaillie, Catherine; Lakshmipathy, Uma

PA Regents of the University of Minnesota, USA

SO PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.
WO 2004050859	A2	20040617	WO 2003-US38811
20031125			
WO 2004050859	A3	20040812	
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW		
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,		

TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
 SN, TD, TG  
 AU 2003298016 A1 20040623 AU 2003-298016  
 20031125  
 US 20060228798 A1 20061012 US 2006-536716  
 20060530  
 PRAI US 2002-429631P P 20021127  
 WO 2003-US38811 W 20031125  
 AB The invention relates to methods of altering gene expression by  
 homologous recombination in a multipotent adult  
 progenitor cell (MAPC). In particular, methods of producing a  
 recombinant MAPC, of correcting a genetic defect in a mammal, of  
 providing a functional and/or therapeutic protein to a mammal,  
 and of  
 transforming and differentiating a MAPC are provided. MAPCs  
 containing an exogenous DNA as well as recombinant MAPCs and  
 their  
 differentiated progeny are also provided. The examples disclose  
 gene  
 targeting and genetic correction of a mutation in the FANCC  
 protein,  
 involved in Fanconi anemia, in mouse MAPCs, followed by  
 transplantation of  
 the corrected cells into FANCC-/- mouse and subsequent reversal  
 of the FANCC  
 deficiency.

=> d his

(FILE 'HOME' ENTERED AT 14:59:11 ON 20 APR 2009)

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:59:20 ON 20 APR 2009

L1 348 S MULTIPOTENT ADULT STEM CELL OR MAPC  
 L2 3 S L1 AND HOMOLOGOUS RECOMBIN?  
 L3 2 DUP REM L2 (1 DUPLICATE REMOVED)

=> s l1 and review

L4 24 L1 AND REVIEW

=> dup rem l4

PROCESSING COMPLETED FOR L4

L5 17 DUP REM L4 (7 DUPLICATES REMOVED)

=> d bib abs 1-

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L5 ANSWER 1 OF 17 BIOSIS COPYRIGHT (c) 2009 The Thomson  
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DUPLICATE 1

AN 2008:636521 BIOSIS

DN PREV200800636520

TI Multipotent adult progenitor cells: their role in wound healing and the treatment of dermal wounds.

AU Herdrich, B. J.; Lind, R. C.; Liechty, K. W. [Reprint Author]

CS Abramson Res Bldg, 3615 Civ Ctr Blvd, Rm 1116E, Philadelphia, PA 19104 USA  
Liechty@email.chop.edu

SO Cytotherapy, (2008) Vol. 10, No. 6, pp. 543-550.  
ISSN: 1465-3249.

DT Article  
General Review; (Literature Review)

LA English

ED Entered STN: 19 Nov 2008  
Last Updated on STN: 27 Nov 2008

AB The use of cellular therapy in the treatment of dermal wounds is currently an active area of investigation. Multipotent adult progenitor cells (MAPC) are an attractive choice for cytotherapy because they have a large proliferative potential, the ability to differentiate into different cell types and produce a variety of cytokines and growth factors important to wound healing. Whole bone marrow (BM) was one of the initial attempts to treat impaired wounds. While it has shown some promise, the low frequency of progenitor cell populations in BM and the large number of inflammatory cells make it less attractive. Multipotent mesenchymal stromal cells (MSC) and endothelial progenitor cells are populations of BM-derived progenitor cells that have been isolated and used to treat chronic wounds with some success. Skin-derived MAPC are another heterogeneous population of progenitor cells present in the skin with the potential to differentiate into skin elements and participate in wound healing. All of these progenitor cell populations are potential sources for cytotherapy of wounds. This review focused on the contribution of adult progenitor cell populations to dermal wound healing and their potential for use in cytotherapy.

L5 ANSWER 2 OF 17 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN  
DUPLICATE 2

AN 2008:383052 BIOSIS

DN PREV200800383051  
 TI Bone marrow - Home of versatile stem cells.  
 AU Ratajczak, Mariusz Z. [Reprint Author]; Zuba-Surma, Ewa K.;  
 Wojakowski,  
 Wojtek; Ratajczak, Janina; Kucia, Magda  
 CS Univ Louisville, Stem Cell Inst, James Graham Brown Canc Ctr,  
 500 S Floyd  
 St, Louisville, KY 40202 USA  
 mzrata01@louisville.edu  
 SO Transfusion Medicine and Hemotherapy, (2008) Vol. 35, No. 3, pp.  
 248-259.  
 ISSN: 1660-3796.  
 DT Article  
 General Review; (Literature Review)  
 LA English  
 ED Entered STN: 9 Jul 2008  
 Last Updated on STN: 9 Jul 2008  
 AB Bone marrow (BM) has been for many years primarily envisioned as  
 the 'home  
 organ' of hematopoietic stem cells (HSC). In this review we  
 will discuss current views of the BM stem cell compartment and  
 present  
 data showing that BM in addition to HSC also contains a  
 heterogeneous  
 population of non-hematopoietic stem cells. These cells have  
 been  
 variously described in the literature as i) endothelial  
 progenitor cells  
 (EPC), ii) mesenchymal stem cells (MSC), iii) multipotent adult  
 progenitor  
 cells (MAPC), iv) marrow-isolated adult multilineage inducible  
 (MIAMI) cells, v) multipotent adult stem cells (MACS) and vi)  
 very small  
 embryonic-like (VSEL) stem cells. It is likely that in many  
 cases similar  
 or overlapping populations of primitive stem cells in the BM  
 were detected  
 using different experimental strategies and hence were assigned  
 different  
 names.

L5 ANSWER 3 OF 17 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All  
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 AN 2008593071 EMBASE  
 TI Purification and culture of human blood vessel-associated  
 progenitor  
 cells.  
 AU Crisan, Mihaela (correspondence); Huard, Johnny; Sun, Bin; Yap,  
 Solomon;  
 Giacobino, Jean-Paul; Casteilla, Louis; Peault, Bruno  
 CS Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA,  
 United States.

AU Huard, Johnny; Peault, Bruno  
 CS McGowan Institute for Regenerative Medicine, Pittsburgh, PA,  
 United States

AU Zheng, Bo; Logar, Alison; Giacobino, Jean-Paul  
 CS Department of Orthopedic Surgery and Molecular Genetics and  
 Biochemistry,  
 Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA,  
 United States.

AU Crisan, Mihaela (correspondence); Huard, Johnny; Zheng, Bo; Sun,  
 Bin; Yap,  
 Solomon; Logar, Alison; Giacobino, Jean-Paul; Peault, Bruno  
 CS Stem Cell Research Center, Children's Hospital of Pittsburgh of  
 UPMC,  
 Pittsburgh, PA, United States.

AU Yap, Solomon  
 CS University of Pittsburgh, Pittsburgh, PA, United States.

AU Casteilla, Louis  
 CS University of Toulouse, Toulouse, France.

SO Current Protocols in Stem Cell Biology, (2008) No. SUPPL. 4, pp.  
 2B.2.1-2B.2.13.  
 Refs: 20  
 ISSN: 1938-8969 E-ISSN: 1941-7322

PB John Wiley and Sons Inc., 111 River Street, Hoboken, NJ  
 07030-5774, United  
 States.

CY United States

DT Journal; General Review; (Review)

FS 029 Clinical and Experimental Biochemistry

LA English

SL English

ED Entered STN: 16 Jan 2009  
 Last Updated on STN: 16 Jan 2009

AB Multilineage progenitor cells, diversely designated as MSC, MAPC  
 , or MDSC, have been previously extracted from long-term  
 cultures of fetal  
 and adult organs (e.g., bone marrow, brain, lung, pancreas,  
 muscle,  
 adipose tissue, and several others). The identity and location,  
 within  
 native tissues, of these elusive stem cells are described here.  
 Subsets  
 of endothelial cells and pericytes, which participate in the  
 architecture  
 of human blood vessels, exhibit, following purification to  
 homogeneity,  
 developmental multipotency. The selection from human tissues,  
 by flow  
 cytometry using combinations of positive and negative cell  
 surface  
 markers, of endothelial and perivascular cells is described  
 here. In



addition, a rare subset of myoendothelial cells that express markers of both endothelial and myogenic cell lineages and exhibit dramatic myogenic and cardiomyogenic potential has been identified and purified from skeletal muscle. The culture conditions amenable to the long-term proliferation of these blood vessel-associated stem cells in vitro are also described. .COPYRGT. 2008 by John Wiley & Sons, Inc.

L5 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2008:88774 CAPLUS

DN 148:324783

TI Stem cells and embryonic stem cells: biological differences

AU Riveros, Dolly Macias; Chagoyan, Juan Carlos Vazquez; Morales, Rogelio

Alonso; Juarez, Marco Cajero

CS Programa de Estudios de Posgrado, Facultad de Medicina Veterinaria y

Zootecnia, Universidad Autonoma del Estado de Mexico, Mexico City, Mex.

SO Veterinaria Mexico (2007), 38(4), 477-501

CODEN: VTERBU; ISSN: 0301-5092

PB Facultad de Medicina Veterinaria y Zootecnia de la Universidad Nacional

Autonoma de Mexico

DT Journal; General Review

LA English/Spanish

AB A review. The stem cells have been classified in three types according to their natural niche of origin, aptitude and differential

function: totipotent, pluripotent and multipotent; the first,

called embryonic stem cells (ES) originate from the morulae; the second,

come from the inner cell mass of the blastocyst (ICM); and the third,

known as multipotent adult progenitor cells (MAPC) are found in some adult tissues. The biol. difference lies in their capabilities to

produce cell lines, the totipotentials have the faculty to originate a

complete organism, the pluripotent can generate all the cellular types

and even the germinal line and the multipotentials can derivate in

specific lineages. The stem cells are able to self-renew, and originate

daughter-cells compromised with certain development routes; they are

characterized for their indefinite division and are morphol. and functionally differentiated. When the stem cells and some progenitor

types are extracted from their natural environment and are grown in vitro, in

suitable medium, can be transfected and remain in an undifferentiated

state without losing their potentiality; thus, when they are reintegrated

to blastocyst receptors they are able to go on with their development.

The study and compilation of information about these biol. qualities of

differential function, as well as their usefulness in homologous recombination and production of animal models that generate recombinant

proteins, applicable for preventive-regenerating medicine and treatment of

diseases, constitute the aim of this work.

RE.CNT 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2007:511777 CAPLUS

DN 147:284597

TI Novel angiogenic therapy using tissue stem cells and materials engineering

AU Sata, Masataka

CS Grad. Sch. of Medicine, The Univ. of Tokyo, Tokyo, Japan

SO Therapeutic Research (2007), 28(3), 325-331

CODEN: THREEEL; ISSN: 0289-8020

PB Raifu Saiensu Shuppan K.K.

DT Journal; General Review

LA Japanese

AB A review. Stem cells are a kind of special cells with the ability of self renewing and differentiation and mainly located in the

marrow. More and more researches have proved that stem cells are related

to the tissue repair. Recent research has found that multipotent adult stem cell is also related to distant

blood vessel repair, remodeling and disease formation. Bone marrow cell

is mobilized and fixed in injured vessel as circulating precursor cell to

differentiate smooth muscle cell and endothelial cell. This maybe the new

therapeutic target for angiopathy. This dissertation introduced the most

novel angiogenic therapy using tissue stem cells and materials engineering. The novel angiogenic therapy includes two main

parts: one is

creation of bio-artificial blood vessel by using blood vessel precursor cell and the other is novel angiogenic therapy using tissue stem cells and low mol. compound

L5 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2007:477682 CAPLUS

DN 147:68870

TI Organogenesis and tissue regeneration using bone marrow stem cells

AU Oki, Masayuki; Ando, Kiyoshi

CS Sch. of Medicine, Dep. of Internal Medicine, Tokai Univ., Japan

SO Annual Review Ketsueki (2007) 46-54

CODEN: ARKNB7

PB Chugai Igakusha

DT Journal; General Review

LA Japanese

AB A review. The topics discussed are (1) plasticity and pluripotency of stem cells; (2) types of stem cells in the bone marrow

including mesenchymal stem cells (MSC), multipotent adult progenitor cells

(MAPC) and hematopoietic stem cells; and (3) tissue regeneration of heart, nerve, bone, liver and blood using MSC and MAPC.

L5 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2006:792443 CAPLUS

DN 146:248292

TI Impairment of the activity of glycosaminoglycan-binding cytokines by

functionally abnormal heparan sulfates: a novel mechanism underlying

disease pathophysiology

AU Gupta, Pankaj

CS Hematology/Oncology Section, Veterans Affairs Medical Center & Hematology-Oncology-Transplantation Division, Department of Medicine,

University of Minnesota Medical School, Minneapolis, USA

SO TheScientificWorld (2006), 6(Jan.), 452-456

CODEN: THESAS; ISSN: 1532-2246

URL:

<http://www.thescientificworld.com/headeradmin/upload/2006.21.83.pdf>

PB TheScientificWorld, Inc.

DT Journal; General Review; (online computer file)

LA English

AB A review. Multipotent adult progenitor cell (MAPC)

derived from normal donors and patients with Hurler syndrome was used to

examine the structure and the functional properties of Hurler heparan

sulfate. Using metabolic labeling of glycosaminoglycans (GAGs), the HS

that accumulates in Hurler MAPC contained a large proportion of small polysaccharide chains. HPLC of fluorescently labeled disaccharides

showed that the disaccharide composition of accumulated HS in Hurler

MAPC was also markedly abnormal. While both normal and Hurler HS were compromised of the six major disaccharide types, the proportions of

all three 6-O-sulfated disaccharides were lower in Hurler HS. There was a

progressive decline in the proportion of UAGlcNS6S with increasing total

accumulation of GAGS. This novel observation suggests that the structural

aberration of HS in Hurler syndrome may continue to worsen with progression of the disease.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 17 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

DUPLICATE 3

AN 2005:318395 BIOSIS

DN PREV200510104054

TI Bone marrow as a home of heterogenous populations of nonhematopoietic stem cells.

AU Kucia, M.; Reca, R.; Jala, V. R.; Dawn, B.; Ratajczak, J.; Ratajczak, M.

Z. [Reprint Author]

CS Univ Louisville, Stem Cell Biol Program, James Graham Brown Canc Ctr,

Louisville, KY 40202 USA

mzrata01@louisville.edu

SO Leukemia (Basingstoke), (JUL 2005) Vol. 19, No. 7, pp. 1118-1127.

CODEN: LEUKED. ISSN: 0887-6924.

DT Article

General Review; (Literature Review)

LA English

ED Entered STN: 17 Aug 2005

Last Updated on STN: 17 Aug 2005

AB Evidence is presented that bone marrow (BM) in addition to CD45(positive)

hematopoietic stem cells contains a rare population of heterogenous

CD45(negative) nonhematopoietic tissue committed stem cells (TCSC). These

nonhematopoietic TCSC (i) are enriched in population of CXCR4(+) CD34(+)

AC133(+) lin(-) CD45(-) and CXCR4(+) Sca-1(+) lin(-) CD45(-) in humans and

mice, respectively, (ii) display several markers of pluripotent stem cells

(PSC) and (iii) as we envision are deposited in BM early in development.

Thus, since BM contains versatile nonhematopoietic stem cells, previous

studies on plasticity trans-dedifferentiation of BM-derived hematopoietic

stem cells (HSC) that did not include proper controls to exclude this

possibility could lead to wrong interpretations. Therefore, in this

spotlight review we present this alternative explanation of 'plasticity' of BM-derived stem cells based on the assumption that BM stem

cells are heterogenous. We also discuss a potential relationship of

TCSC/PSC identified by us with other BM-derived CD45(negative) nonhematopoietic stem cells that were recently identified by

other

investigators (eg MSC, MAPC, USSC and MIAMI cells). Finally, we discuss perspectives and pitfalls in potential application of these cells

in regenerative medicine.

L5 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2006:154226 CAPLUS

DN 145:59671

TI Adult stem cells and possible mechanisms of its differentiation-editorial

AU Zhou, Zhuoyan; Yang, Mo; Jiang, Yuehua

CS Medical College, Jinan University, Guangzhou, 510632, Peop. Rep. China

SO Zhongguo Shiyen Xueyexue Zazhi (2005), 13(3), 353-357  
CODEN: ZSXZAF; ISSN: 1009-2137

PB Zhongguo Shiyen Xueyexue Zazhishe

DT Journal; General Review

LA Chinese

AB A review. Adult stem cells are the multi-potential cells, which exist in fetal and adult tissues. It can reproduce itself (undergo

self-renewal) or give rise to more specialized (differentiated) cells.

Under certain inducing conditions, adult stem cells can acquire the

ability to differentiate into different tissue cells.

Multipotent adult

progenitor cells (MAPC), an alternative name of adult stem cell given by Catherine Verfaillie, existing in bone marrow, can differentiate

into cells with characteristics of mesodermal, neuroectodermal, and

endodermal lineages in vitro at the single-cell level. MAPC can also contribute to most cell types when injected into the blastocyst.

Adult stem cell differentiation implies that different cell lineages are

derived from a single initial cell. All differentiated cell types are

functional in vitro and in vivo and engraftment is robust and persistent

in the physiol. and pathol. situations. The possible mechanisms may

underlie the differentiation: various tissue-specific stem cells are

present in different niche that imparts signals to activate a novel

genetic program needed for the new cell fate. And true multi-potential

stem cells persist in postnatal life. In the future, multi-potent adult

stem cells might then be used for therapies of degenerative or genetic

disorders of multiple different organs.

L5 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 4

AN 2004:1064432 CAPLUS

DN 142:131212

TI Stem cells today: B1. bone marrow stem cells

AU Edwards, Bob

CS Reproductive BioMedicine Online, Dray Drayton, Cambridge, CB3 8DB, UK

SO Reproductive BioMedicine Online (2004), 9(5), 541-583

CODEN: RBOEA6; ISSN: 1472-6483

PB Reproductive Healthcare Ltd.

DT Journal; General Review

LA English

AB A review. This is the 2nd in a series of 4 devoted to the anal. of recent studies on stem cells. The 1st considered embryo stem cells

(ES). This review covers bone marrow stem cells. They are analyzed initially in a historical perspective, and then in relation to

foundation studies in the later 20th century before a detailed anal. is

presented on very recent studies. Methods of identifying, culturing,

expanding and grafting stem cells are described, including the separation of

hemopoietic and mesenchyme cell lines (HSC and MSC) and recent more

detailed analyses using numerous CD and other markers to identify very

small subsets of stem cells such as multipotent adult progenitor cells (

MAPC) and bone marrow stromal stem cells (BMSSC) from MSC.  
Queries arising on the immense potential of these stem cell  
lines due to  
the discovery of epigenetic factors and cell fusions influencing  
their  
development and potency are described. A section on cord blood  
stem cells  
is followed by a detailed discussion on the modern situation  
regarding the  
clin. use of stem cells, its recent setbacks due to epigenetic  
factors,  
different approaches to the discovery of a highly multipotent  
bone marrow  
stem cell, and a brief description of embryol. approaches to  
identifying  
the basic bone marrow stem cell in very early mammalian embryos.  
RE.CNT 195 THERE ARE 195 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 17 BIOSIS COPYRIGHT (c) 2009 The Thomson  
Corporation on

STN

DUPLICATE 5

AN 2004:322633 BIOSIS

DN PREV200400323444

TI Bone and fat - Old questions, new insights.

AU Gimble, Jeffrey M. [Reprint Author]; Nuttal, Mark E.

CS Pennington Biomed Res CtrStem Cell Lab, Louisiana State Univ,  
6400 Perkins

Rd, Baton Rouge, LA, 70808, USA

gimblejm@pbrc.edu

SO Endocrine, (March 2004) Vol. 23, No. 2-3, pp. 183-188. print.

ISSN: 1355-008X.

DT Article

General Review; (Literature Review)

LA English

ED Entered STN: 21 Jul 2004

Last Updated on STN: 21 Jul 2004

AB Until recently, adipose tissue was considered to serve only as a  
triglyceride reservoir and was relegated to a passive endocrine  
role.

With the discovery of leptin and other adipokines, adipose  
tissue is now

recognized as an active participant in systemic metabolism. This  
review focuses on the complex relationship existing between  
adipose tissue and bone metabolism and differentiation. It  
explores the

paradigms that have shaped the past decade's research and what  
these

findings forecast for the future. Particular attention is given  
to the

multipotent adult stem cell

populations that reside within bone and fat. These adult stem  
cells have

critical importance to the emerging field of tissue engineering and regenerative medicine.

L5 ANSWER 12 OF 17 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on

STN

DUPLICATE 6

AN 2004:386407 BIOSIS

DN PREV200400386308

TI Heterogeneous populations of bone marrow stem cells - are we spotting on

the same cells from the different angles?.

AU Ratajczak, Mariusz Z. [Reprint Author]; Kucia, Magda; Majka, Marcin; Reca,

Ryan; Ratajczak, Janina

CS James Graham Brown Canc CtrStem Cell Biol Program, Univ Louisville, 529 S

Jackson St, Louisville, KY, 40202, USA

mzrata01@louisville.edu

SO Folia Histochemica et Cytobiologica, (2004) Vol. 42, No. 3, pp. 139-146.

print.

CODEN: FHCYEM. ISSN: 0239-8508.

DT Article

General Review; (Literature Review)

LA English

ED Entered STN: 29 Sep 2004

Last Updated on STN: 29 Sep 2004

AB Accumulated evidence suggests that in addition to hematopoietic stem cells

(HSC), bone marrow (BM) also harbors endothelial stem cells (ESC),

mesenchymal stem cells (MSC), multipotential adult progenitor cells (

MAPC), pluripotent stem cells (PCS) as well as tissue committed stem cells (TCSC) recently identified by us. In this review we discuss the similarities and differences between these cell populations.

Furthermore, we will present the hypothesis that all of these versatile BM

derived stem cells are in fact different subpopulations of TCSC.

These

cells accumulate in bone marrow during ontogenesis and being a mobile

population of cells are released from BM into peripheral blood after

tissue injury to regenerate damaged organs. Furthermore, since BM is a

"hideout" for TCSC, their presence in preparations of bone marrow derived

mononuclear cells should be considered before experimental evidence is



interpreted simply as trans-differentiation or plasticity of HSC.  
Finally, our observation that the number of TCSC accumulate in  
the bone  
marrow of young animals and their numbers decrease during  
senescence  
provides a new insight into aging and may explain why the  
regeneration  
processes becomes less effective in older individuals.

L5 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2004:339356 CAPLUS

DN 140:388923

TI The bone marrow: a reserve of stem cells able to repair various  
tissues?

AU Cavazzana-Calvo, M.; Lagresle, C.; Andre-Schmutz, I.;

Hacein-Bey-Abina, S.

CS Departement de biotherapie, Fr.

SO Annales de Biologie Clinique (2004), 62(2), 131-138

CODEN: ABCLAI; ISSN: 0003-3898

PB John Libbey Eurotext

DT Journal; General Review

LA French

AB A review. Hematopoietic stem cells (HSC) have been widely used  
for autologous and allogeneic transplantation during decades,  
although

little was known about their migration, survival, self-renewal  
and

differentiation process. Their sorting by the CD34+ marker they  
express

at the cell surface in human has been challenged by the recent  
discovery

of HSC in the CD34- compartment that may precede CD34+ HSC in the  
differentiation process. Until recently, stem cells present in  
the bone

marrow were thought to be specific for hematopoiesis. Some  
expts.

including clin. trials showing the formation of various tissues,  
muscle,

neural cells and hepatocytes for instance, after transplantation  
of

medullar cells, have challenged this dogma. In fact, the proofs  
of such a

transdifferentiation process by HSC are still missing and the  
observations

may result from the differentiation of other multipotent stem  
cells

present in the bone marrow, such as mesenchymal stem cells and  
more

primitive multi-potent adult progenitor cells (MAPC) and side  
population (SP) cells.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 17 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

AN 2003323882 EMBASE

TI [Plasticity of adult stem cells].  
Plasticite des cellules souches adultes.

AU Turhan, Ali (correspondence)

CS U. de Therapie Cell. et Inserm U362, Institut Gustave-Roussy, 39, rue Camille-Desmoulins, 94805 Villejuif Cedex, France. turali@igr.fr

SO Hematologie, (Mar 2003) Vol. 9, No. 2, pp. 105-116.  
Refs: 66  
ISSN: 1264-7527 CODEN: HEMAF2

CY France

DT Journal; General Review; (Review)

FS 025 Hematology

LA French

SL English; French

ED Entered STN: 28 Aug 2003  
Last Updated on STN: 28 Aug 2003

AB During the recent years, experimental data obtained in the murin system led to a drastic change in our classical concepts of adult stem cells.  
Until recently, these cells, in addition to their classical self-renewal and differentiation abilities, were supposed to exhibit tissue-specificity. This concept has been challenged by bone marrow transplantation experiments in demonstrating that not marrow cells could generate not only hematopoietic cells but also muscle cells, hepatic cells or neuronal cells in lethally irradiated recipients.  
Conversely, muscle cells or brain cells could generate hematopoietic cells upon transplantation. The term "plasticity" has been coined to explain this phenomenon which could be due to the persistence in adult tissues, of stem cells with multi-differentiation ability or to the "transdifferentiation" ability of some adult cells committed to differentiation, under the influence of some environmental cues, a phenomenon which is known to occur in vitro. The phenotype of cells at the origin of «plasticity» is currently the subject of investigations and controversies in many laboratories. If the functional nature of several types of cells generated after bone marrow transplantation has been

demonstrated in mice, experiments using clonal transplantations have given conflicting results. The relationship of the cells at the origin of the stem cells plasticity with a new type of mesodermal cell designed under the term of "multipotent adult progenitor cell" (MAPC) remains to be determined. The discovery of this latter is a major advance in this field as the MAPC have isolated from the adult bone marrow and present certain characteristics of embryonic stem cells with the demonstration of their totipotency towards many tissues, including hematopoiesis. The discovery of the adult stem cell plasticity phenomenon in general, whether due to the programming of adult stem cells under the influence of some specific environmental cues or to the persistence in adult tissues of stem cells with embryonal characteristics, represent a major change in our concepts of stem and developmental biology. Many in vitro and in vivo experiments will be necessary to determine if the data generated by the use of adults stem cells in mice could be translated to humans in order to develop future cell therapy protocols.

L5 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN  
AN 2002:109123 CAPLUS  
DN 136:291972  
TI Putting the neo into neoangiogenesis  
AU Moore, Malcolm A. S.  
CS Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA  
SO Journal of Clinical Investigation (2002), 109(3), 313-315  
CODEN: JCINAO; ISSN: 0021-9738  
PB American Society for Clinical Investigation  
DT Journal; General Review  
LA English  
AB A review. The research of Reyes, M.; et al. (2002) on the participation of endothelial cells in new blood vessel formation in normal and pathol. states, including tumor neoangiogenesis, is reviewed with commentary and refs. A unique cell in human and rodent postnatal marrow, designated the multipotent adult progenitor cell (MAPC), was identified. MAPCs were selected by depleting adult bone marrow of hematopoietic cells expressing CD45 and glycophorin-A, followed by

long-term culture of fibronectin with EGF and PDGF under low serum conditions. The potential of human MAPCs , obtained after 20-65 PD, to form functional endothelium, was evaluated. The results showed that the cells form vascular tubes when plated on Matrigel and upregulate angiogenic receptors and VEGF in response to hypoxia. A comparison of MAPC with embryonic stem cells and cells generated by therapeutic cloning is presented.

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2002:396338 CAPLUS

DN 137:319820

TI Bone marrow stromal cells as targets for gene therapy

AU Van Damme, An; Vanden Driessche, Thierry; Collen, Desire; Chuah, Marinee

K. L.

CS Center for Transgene Technology and Gene Therapy, Flanders Interuniversity

Institute for Biotechnology-University of Leuven, Louvain, B-3000, Belg.

SO Current Gene Therapy (2002), 2(2), 195-209

CODEN: CGTUAH; ISSN: 1566-5232

PB Bentham Science Publishers Ltd.

DT Journal; General Review

LA English

AB A review. The bone marrow (BM) is composed of the non-adherent hematopoietic and adherent stromal cell compartment. This adherent BM

stromal cell fraction contains pluripotent mesenchymal stem cells (MSCs)

and differentiated mesenchymal BM stromal cells. The MSCs self-renew by

proliferation while maintaining their stem-cell phenotype and give rise to

the differentiated stromal cells which belong to the osteogenic, chondrogenic, adipogenic, myogenic and fibroblastic lineages. A more

primitive adherent stem cell was recently identified, the multipotent

adult progenitor cell (MAPC) or mesodermal progenitor cell, which co-purifies with MSCs. These MAPCs differentiate into MSCs,

endothelial, epithelial and even hematopoietic cells. BM stroma cells,

including the primitive pluripotent MSCs and MAPCs, are attractive targets

for cell and gene therapy. The BM stromal cell population and its

multipotent stem cells can be engineered to secrete a series of different

proteins in vitro and in vivo that could potentially treat a variety of

serum protein deficiencies and other genetic or acquired diseases,

including bone, cartilage and BM stromal disorders or even cancer.

RE.CNT 82        THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5    ANSWER 17 OF 17    EMBASE    COPYRIGHT (c) 2009 Elsevier B.V. All rights

reserved on STN

AN    1997141519    EMBASE

TI    Two-component signal transducers and MAPK cascades.

AU    Wurgler-Murphy, Susannah M. (correspondence); Saito, Haruo

CS    Division of Tumor Immunology, Dana-Farber Cancer Institute, Harvard

Medical School, Boston, MA 02115, United States.

haruo\_saito@dfci.harvard.

edu

AU    Wurgler-Murphy, Susannah M. (correspondence)

CS    Division Tumor Immunology, Dana-Farber Cancer Institute, Boston, MA 02115,

United States.

SO    Trends in Biochemical Sciences, (May 1997) Vol. 22, No. 5, pp. 172-176.

Refs: 38

ISSN: 0968-0004    CODEN: TBSCDB

PUI   S 0968-0004(97)01036-0

CY    United Kingdom

DT    Journal; General Review; (Review)

FS    029        Clinical and Experimental Biochemistry

004        Microbiology: Bacteriology, Mycology, Parasitology and

Virology

LA    English

SL    English

ED    Entered STN: 29 May 1997

Last Updated on STN: 29 May 1997

AB    Two-component signal transducers, which are characterized by the histidine-to-aspartate phospho-transfer mechanism, were once thought to be

restricted to prokaryotes. They have, however, now been identified in

diverse eukaryotic species including plant, fungus, yeast and slime mold,

In yeast, a two-component osmosensor has been found to regulate a mitogen-activated protein kinase (MAPK) cascade, a ubiquitous eukaryotic signaling module.

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	ENTRY	SESSION
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	ENTRY	SESSION
CA SUBSCRIBER PRICE	-8.20	
-8.20		

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 LAST RELOADED: Apr 17, 2009 (20090417/UP).

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FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:59:20 ON 20 APR 2009

L1	348 S MULTIPOTENT ADULT STEM CELL OR MAPC
L2	3 S L1 AND HOMOLOGOUS RECOMBIN?
L3	2 DUP REM L2 (1 DUPLICATE REMOVED)
L4	24 S L1 AND REVIEW
L5	17 DUP REM L4 (7 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 15:04:20 ON 20 APR 2009

=> s l1 and pY,=2002  
 '2002' NOT A VALID FIELD CODE

	0 MULTIPOTENT
	0 ADULT
	0 STEM
	15 CELL
	0 MULTIPOTENT ADULT STEM CELL
	(MULTIPOTENT(W)ADULT(W)STEM(W)CELL)
	1 MAPC
	0 PY,=2002
L6	0 L1 AND PY,=2002

=> FIL BIOSIS CAPLUS EMBASE		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.63	84.28
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	
-8.20		

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=> s l1 and pY<=2002  
L7 135 L1 AND PY<=2002

=> dup rem l7  
PROCESSING COMPLETED FOR L7  
L8 88 DUP REM L7 (47 DUPLICATES REMOVED)

=> s l8 and vector  
L9 0 L8 AND VECTOR

=> s l8 and recombina?  
L10 0 L8 AND RECOMBIN?

=> d bib abs l8 1-10

L8 ANSWER 1 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson  
Corporation on STN  
DUPLICATE 1  
AN 2002:496942 BIOSIS  
DN PREV200200496942  
TI Multipotent progenitor cells can be isolated from postnatal  
murine bone  
marrow, muscle, and brain.  
AU Jiang, Yuehua; Vaessen, Ben; Lenvik, Todd; Blackstad, Mark;  
Reyes,  
Morayma; Verfaillie, Catherine M. [Reprint author]  
CS Department of Medicine, University of Minnesota, 422 Delaware  
Street SE,  
MMC 716, Minneapolis, MN, 55455, USA  
verfa001@umn.edu  
SO Experimental Hematology (Charlottesville), (August, 2002) Vol.  
30, No. 8, pp. 896-904. print.  
CODEN: EXHMA6. ISSN: 0301-472X.  
DT Article  
LA English  
ED Entered STN: 18 Sep 2002  
Last Updated on STN: 18 Sep 2002  
AB Objective: Recent studies have shown that cells from bone marrow  
(BM),  
muscle, and brain may have greater plasticity than previously  
known. We

have identified multipotent adult progenitor cells (MAPC) in postnatal human and rodent BM that copurify with mesenchymal stem cells (MSC). BM MAPC proliferate without senescence and differentiate into mesodermal, neuroectodermal, and endodermal cell types. We hypothesized that cells with characteristics similar to BM MAPC can be selected and cultured from tissues other than BM.

**Materials and Methods:** BM, whole brain, and whole muscle tissue was obtained from mice. Cells were plated on Dulbecco modified Eagle medium supplemented with 2% fetal calf serum and 10 ng/mL epidermal growth factor (EGF), 10 ng/mL platelet-derived growth factor (PDGF-BB), and 1000 units/mL leukemia inhibitory factor (LIF) for more than 6 months. Cells were maintained between 0.5 and 1.5X10<sup>3</sup> cells/cm<sup>2</sup>. At variable time points, we tested cell phenotype by FACS and evaluated their differentiation into endothelial cells, neuroectodermal cells, and endodermal cells in vitro. We also compared the expressed gene profile in BM, muscle, and brain MAPC by Affimetrix gene array analysis. Results: Cells could be cultured from BM, muscle, and brain that proliferated for more than 70 population doublings (PDs) and were negative for CD44, CD45, major histocompatibility complex class I and II, and c-kit. Cells from the three tissues differentiated to cells with morphologic and phenotypic characteristics of endothelium, neurons, glia, and hepatocytes. The expressed gene profile of cells derived from the three tissues was identical ( $r^2 > 0.975$ ). Conclusions: This study shows that cells with MAPC characteristics can be isolated not only from BM, but also from brain and muscle tissue. Whether MAPC originally derived from BM are circulating or all organs contain stem cells with MAPC characteristics currently is being studied. Presence of MAPC in multiple tissues may help explain the "plasticity" found in multiple adult tissues.



AN 2002:174753 BIOSIS  
 DN PREV200200174753  
 TI Origin of endothelial progenitors in human postnatal bone marrow.  
 AU Reyes, Morayma; Dudek, Arkadiusz; Jahagirdar, Balkrishna; Koodie, Lisa;  
 Marker, Paul H.; Verfaillie, Catherine M. [Reprint author]  
 CS University of Minnesota, 422 Delaware Street SE, MMC 716, Minneapolis, MN, 55455, USA  
 verfa001@umn.edu  
 SO Journal of Clinical Investigation, (February, 2002) Vol. 109, No. 3, pp. 337-346. print.  
 CODEN: JCINAO. ISSN: 0021-9738.  
 DT Article  
 LA English  
 ED Entered STN: 6 Mar 2002  
 Last Updated on STN: 6 Mar 2002  
 AB This study demonstrates that a CD34-, vascular endothelial cadherin- (VE-cadherin-), AC133+, and fetal liver kinase+ (Flk1+) multipotent adult progenitor cell (MAPC) that copurifies with mesenchymal stem cells from postnatal human bone marrow (BM) is a progenitor for angioblasts. In vitro, MAPCs cultured with VEGF differentiate into CD34+, VE-cadherin+, Flk1+ cells-a phenotype that would be expected for angioblasts. They subsequently differentiate into cells that express endothelial markers, function in vitro as mature endothelial cells, and contribute to neoangiogenesis in vivo during tumor angiogenesis and wound healing. This in vitro model of preangioblast-to-endothelium differentiation should prove very useful in studying commitment to the angioblast and beyond. In vivo, MAPCs can differentiate in response to local cues into endothelial cells that contribute to neoangiogenesis in tumors. Because MAPCs can be expanded in culture without obvious senescence for more than 80 population doublings, they may be an important source of endothelial cells for cellular pro- or anti-angiogenic therapies.

L8 ANSWER 3 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN  
 AN 2002:109123 CAPLUS  
 DN 136:291972  
 TI Putting the neo into neoangiogenesis  
 AU Moore, Malcolm A. S.  
 CS Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA

SO Journal of Clinical Investigation (2002), 109(3), 313-315  
CODEN: JCINAO; ISSN: 0021-9738  
PB American Society for Clinical Investigation  
DT Journal; General Review  
LA English  
AB A review. The research of Reyes, M.; et al. (2002) on the participation of endothelial cells in new blood vessel formation in normal and pathol. states, including tumor neoangiogenesis, is reviewed with commentary and refs. A unique cell in human and rodent postnatal marrow, designated the multipotent adult progenitor cell (MAPC), was identified. MAPCs were selected by depleting adult bone marrow of hematopoietic cells expressing CD45 and glycophorin-A, followed by long-term culture of fibronectin with EGF and PDGF under low serum conditions. The potential of human MAPCs , obtained after 20-65 PD, to form functional endothelium, was evaluated. The results showed that the cells form vascular tubes when plated on Matrigel and upregulate angiogenic receptors and VEGF in response to hypoxia. A comparison of MAPC with embryonic stem cells and cells generated by therapeutic cloning is presented.  
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN  
AN 2002:396338 CAPLUS  
DN 137:319820  
TI Bone marrow stromal cells as targets for gene therapy  
AU Van Damme, An; Vanden Driessche, Thierry; Collen, Desire; Chuah, Marinee  
K. L.  
CS Center for Transgene Technology and Gene Therapy, Flanders Interuniversity Institute for Biotechnology-University of Leuven, Louvain, B-3000, Belg.  
SO Current Gene Therapy (2002), 2(2), 195-209  
CODEN: CGTUAH; ISSN: 1566-5232  
PB Bentham Science Publishers Ltd.  
DT Journal; General Review  
LA English  
AB A review. The bone marrow (BM) is composed of the non-adherent hematopoietic and adherent stromal cell compartment. This adherent BM stromal cell fraction contains pluripotent mesenchymal stem cells (MSCs)

and differentiated mesenchymal BM stromal cells. The MSCs self-renew by proliferation while maintaining their stem-cell phenotype and give rise to the differentiated stromal cells which belong to the osteogenic, chondrogenic, adipogenic, myogenic and fibroblastic lineages. A more primitive adherent stem cell was recently identified, the multipotent adult progenitor cell (MAPC) or mesodermal progenitor cell, which co-purifies with MSCs. These MAPCs differentiate into MSCs, endothelial, epithelial and even hematopoietic cells. BM stroma cells, including the primitive pluripotent MSCs and MAPCs, are attractive targets for cell and gene therapy. The BM stromal cell population and its multipotent stem cells can be engineered to secrete a series of different proteins in vitro and in vivo that could potentially treat a variety of serum protein deficiencies and other genetic or acquired diseases, including bone, cartilage and BM stromal disorders or even cancer.

RE.CNT 82        THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD  
                 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8    ANSWER 5 OF 88    BIOSIS    COPYRIGHT (c) 2009 The Thomson  
Corporation    on STN

AN    2002:400175    BIOSIS

DN    PREV200200400175

TI    Ex vivo and in vivo primitive and definitive hematopoiesis from a  
non-hematopoietic stem cell.

AU    Reyes, M.; Verfaillie, C.; Koodie, L.; Lund, T.; Lenvik, T.;  
Jahagirdar,  
B.

SO    Experimental Hematology (Charlottesville), (June, 2002) Vol. 30,  
No. 6 Supplement 1, pp. 42. print.

Meeting Info.: 31st Annual Meeting of the International Society  
for  
Experimental Hematology. Montreal, Quebec, Canada. July 05-09,  
2002.

CODEN: EXHMA6. ISSN: 0301-472X.

DT    Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA    English

ED    Entered STN: 24 Jul 2002

Last Updated on STN: 29 Aug 2002

L8    ANSWER 6 OF 88    BIOSIS    COPYRIGHT (c) 2009 The Thomson  
Corporation    on STN

AN 2003:283255 BIOSIS  
 DN PREV200300283255  
 TI HUMAN AND RAT DERIVED MULTIPOTENT ADULT PROGENITOR CELLS ( MAPC ) SURVIVE AND EXPRESS NEURAL MARKERS WHEN TRANSPLANTED INTO NEONATAL RATS.  
 AU Ortiz-Gonzalez, X. R. [Reprint Author]; Keene, C. D. [Reprint Author];  
 Reyes, M. [Reprint Author]; Nan, Z. H. [Reprint Author]; Duan, W. M. [Reprint Author]; Verfaillie, C. M. [Reprint Author]; Low, W. C. [Reprint Author]  
 CS Neurosurgery, Medicine, Graduate Program in Neuroscience, Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA  
 SO Society for Neuroscience Abstract Viewer and Itinerary Planner, ( 2002) Vol. 2002, pp. Abstract No. 237.19.  
<http://sfn.scholarone.com.cd-rom>.  
 Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience.  
 Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.  
 DT Conference; (Meeting)  
 Conference; (Meeting Poster)  
 Conference; Abstract; (Meeting Abstract)  
 LA English  
 ED Entered STN: 19 Jun 2003  
 Last Updated on STN: 19 Jun 2003  
 AB Multipotent Adult Progenitor Cells (MAPCs) have been shown to generate tissue derivatives from each of the three embryonic germ layers both in vivo and in vitro.)We intend to test the potential of these bone marrow-derived cells as a source of tissue for CNS cellular repair and replacement therapies. In order to study the survival and differentiation of MAPCs into the mammalian postnatal brain in vivo, we transplanted undifferentiated rat or human MAPCs intracerebroventricularly in neonatal (P1-P3) rats. Animals were sacrificed at 2, 4 or 12 weeks of age, and immunofluorescent studies were performed to evaluate expression of neural markers in vivo by donor-derived cells. Human MAPCs were found in the hippocampal formation and periventricular areas. We were able to detect human MAPCs-derived cells that were double labeled for the human nuclear membrane antigen and GFAP or NeuN (markers for astrocytes and neurons,

respectively). Rat MAPC-derived cells showed better survival and neural differentiation, both immunohistochemically and morphologically. eGFP+ rat MAPC-derived cells expressing NeuN or GFAP were also found, predominantly within the hippocampal formation.

These preliminary studies support the potential of MAPCs for the development of neural transplantation therapies.

L8 ANSWER 7 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN  
AN 2003:336702 BIOSIS  
DN PREV200300336702  
TI Neuralization of Hematopoietic Stem Cells; Neurospheres Derived from Human Umbilical Cord Blood.  
AU Reems, Jo Anna [Reprint Author]; Hagman, Derek K. [Reprint Author];  
Lingohr, Melissa K. [Reprint Author]; Rhodes, Christopher J. [Reprint Author]  
CS Puget Sound Blood Center/Northwest Tissue Center, Seattle, WA, USA  
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2004. print.  
Meeting Info.: 44th Annual Meeting of the American Society of Hematology.  
Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)  
LA English  
ED Entered STN: 23 Jul 2003  
Last Updated on STN: 23 Jul 2003  
AB Observations of stem cell plasticity have increasingly been reported for a  
wide range of embryonic, neonatal and adult tissues. In our own investigation, ex vivo culture of the light-density fraction of nucleated  
cells isolated from human umbilical cord blood was carried out in two  
stages, which repeatedly produced an adherent cell population that  
exhibited neural morphology. Initially, these cells were maintained in a  
serum-enriched media for up to 72 hours. Following this, the cells were  
sub-cultured at densities of 0.6-1.0x10<sup>6</sup> cells/ml in a serum-free neuralization media supplemented with basic fibroblastic growth factor  
(bFGF) and B27 for seven days. As a control, cord blood cells were also

sub-cultured in Myelocult H5100 or left in the serum-enriched media following the 72-hour incubation. Cell densities at  $1.0 \times 10^6$  failed to produce an expanding adherent cell population. Neuralization of the adherent layer of cells occurred in the presence of bFGF+B27 and was confirmed via RT-PCR for the expression of the glial fibrillary acidic protein (GFAP) marker for astrocytes and microtubule-associated protein-2 (MAP2) for neurons. Fluorescent activated cell sorting (FACS) and subsequent culturing assays indicated that the neuralized cell population was derived from the CD34- cell fraction. Cord blood cells sub-cultured in Myelocult H5100 or left in the serum-enriched media following the 72-hour incubation period failed to generate neuralized cells. However, cells left in the serum-based media did produce an expanding, passage-able adherent layer characteristic of the mesenchymal stem cell (MSC) population. Two distinct types of cells, both fibroid-like and osteoclast-like cells were observed. Interestingly, exposure of the MSC-like adherent cells to the neuralization media did produce a small number of neural-like cells. However, FACS of the MSC-like cells using the CD105 and CD51/61 markers failed to produce neuralized cells. It remains to be determined if the recently described multipotent adult progenitor cells (MAPC) that co-purify with the MSC population represent the source of these neuralizing cells in hematopoietic tissues. Finally, cord blood cultures extended out to 12 days, exhibited an abundance of cells clustered into balls, freely suspended in the media above the adherent layer. When transferred to new culture flasks containing neuralization media, these clusters typically adhere rapidly and reconstitute a new neuralized adherent layer. In one instance, however, the cell clusters produced were maintained in suspension, and using confocal microscopy stained positively for the neural markers

neurogenin-3 (Ngn3) and nestin, and for the proliferation marker Ki-67.

Presumed to be neurospheres containing neuro/epithelial progenitors, these clusters exhibited spontaneous differentiation into structures exhibiting astrocyte morphology and positive staining for GFAP/Ngn3 and insulin receptor substrate-2 (IRS2). Together these results indicate that stem cells contained within umbilical cord blood have the potential to differentiate into cells that express markers of neural development.

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AN 2003:337290 BIOSIS

DN PREV200300337290

TI Purification of MSC from Mouse Compact Bone.

AU Short, Brenton J. [Reprint Author]; Brouard, Nathalie [Reprint Author];

Simmons, Paul J. [Reprint Author]

CS Stem Cell Biology Laboratory, Peter MacCallum Cancer Institute, East

Melbourne, VIC, Australia

SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 225. print.

Meeting Info.: 44th Annual Meeting of the American Society of Hematology.

Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 23 Jul 2003

Last Updated on STN: 23 Jul 2003

AB Adult mammalian bone marrow (BM) contains at least two distinct populations of stem cells; those of the hematopoietic lineage and a second

population termed mesenchymal (MSC) or marrow stromal stem cells (fibroblast colony-forming cells; CFU-F) which represent stem cells for

non-haemopoietic tissues within the BM. The progeny of these cells play a

key role in skeletal homeostasis as well as providing functional support

for the proliferation and differentiation of hematopoietic cells. Recent

studies have suggested that cells co-purifying with MSC may be multipotent

adult precursor cells (MAPC) capable of generating cells of all

three germ layers and subsequently all somatic cell types. MSC have been implicated as targets in a variety of cellular therapies for the treatment of defects of the haemopoietic and skeletal systems and as vehicles for gene therapies. Much of our understanding of the biology of these cells is based upon in vitro studies of culture selected and expanded cells. In contrast little is known about the cellular and molecular characteristics of MSC in vivo. In the mouse, major barriers to the study of MSC include their low incidence within the BM and the lack of phenotypic markers to facilitate their identification and isolation. We now describe a robust methodology for the prospective isolation of MSC in adult murine BM. In accord with previous studies, the incidence of CFU-F in mouse compact bone (CB) was significantly higher than that in BM ( $2689 \pm 58$  vs.  $102 \pm 80$  colonies/ $10^6$  cells respectively,  $n=5$ ). Approximately 75% of total femoral CFU-F were recovered in the CB fraction. Based on these data we developed a methodology for the purification of CFU-F from mouse CB based on sequential negative selection using a panel of antibodies to cell surface molecules on mature haemopoietic lineages (Lin-) followed by positive selection using fluorescence-activated cell sorting (FACS). The CB lin- fraction, representing  $5.2 \pm 0.5$  % of the input population ( $n=28$ ) exhibited a colony-forming efficiency (CFE) of  $23 \pm 2.6$  colonies/ $10^3$  cells plated ( $n=4$ ). Dual colour FACS of the Lin- CB fraction stained with antibodies to CD45 and Sca-1 resolved a discrete subpopulation of Sca-1brightCD45-Lin- cells with a CFE by limit-dilution analysis of  $11.3 \pm 2$ %. Analysis of clones derived from single Sca-1brightCD45-Lin- cells indicate that these MSC cells have high although variable proliferative potential (50-125 population doublings) whilst maintaining at least a tripotential differentiative capacity as assessed by in vitro adipogenic, chondrogenic and osteogenic differentiation assays. Neither



freshly isolated nor cultured MSC contributed to the haemopoietic lineage following transplant into ablated recipients. Depletion of CD31+ cells from the Sca-1brightCD45- fraction increased the CFE to approximately 1 per 3 cells plated, with all assayable CFU-F recovered in the CD31- fraction. While this is by far the most highly enriched population of murine CFU-F yet described, current studies exploiting further phenotypic heterogeneity within this Sca-1brightCD45-Lin-CD31- population will likely yield a homogeneous population of MSC. These studies represent the first description of a phenotype containing a highly enriched population of mouse MSC and provide an important prerequisite not only for fundamental studies of the cellular and molecular biology of these poorly characterised stem cells but also for the development of a mouse model to investigate the utility of BM derived MSC in a range of cellular therapies.

L8 ANSWER 9 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN  
AN 2003:367607 BIOSIS  
DN PREV200300367607  
TI Transdifferentiation of Human Haemopoietic Lineage Negative Bone Marrow Cells to Neural Cells by Cytokines and Chemical Inducing Agents.  
AU Tao, Helen [Reprint Author]; Rao, Renuka S. [Reprint Author]; Ma, David D. F. [Reprint Author]  
CS Department of Haematology and Haematopoietic Stem Cell Transplantation, St Vincent's Hospital, Sydney, NSW, Australia  
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 4123. print.  
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)  
LA English  
ED Entered STN: 13 Aug 2003  
Last Updated on STN: 13 Aug 2003

AB Adult stem cell plasticity is currently the subject of intensive research,  
as it holds immense potentials for treatment of various human diseases.  
several groups have demonstrated the presence of a type of stem cells in  
the adult human bone marrow termed mesenchymal stem cells (MSCs) multipotent adult progenitor cells (MAPC), capable of differentiating into cells of ectoderm, mesoderm and endoderm origins.  
interestingly these cells have the potential to differentiate into neuronal like cells in vitro thus raising the possibility of stem cell therapy for neural degenerative disorders such as stroke and Parkinson's disease. Although a variety of reagents have been reported for inducing neuronal differentiation, the most effective agent(s) for inducing this lineage switch and the optimal culture conditions for long term maintenance remain to be defined. in this study we have induced neuronal differentiation of haemopoietic lineage negative BM cells using a cocktail of growth factors including bFGF, EGF and PDGF. The efficiency of neuronal induction and its maintenance in culture are compared to the previously reported method of induction using butylated hydroxyanisole (BHA) and dimethylsulfoxide (DMSO). BM samples from individuals collected after consent, were subjected to gradient centrifugation followed by plastic adherence or immunomagnetic bead sorting to obtain cd34-/14-/45-/glycophorin-A- cells. These cells were grown in DMEM based culture medium supplemented with or without fetal calf serum. After several passages cells were induced with either BHA/DMSO or the cocktail of growth factors. Morphologically, induction with BHA/DMSO resulted in a uniform neuronal-like cell population within 6 hrs. Also expression of neuronal specific markers and genes such as NSE, NeuN, NF-M, MAP2, b tubulin III and tau could be detected. However these cells could not be maintained in culture for more than 7 days. In contrast the cells induced

with the combination of growth factors showed a gradual change in morphology over a period of few weeks but were more stable and have been

maintained in culture for 2-3 months without loss of neuronal properties.

The growth factors induced differentiation, also produced a heterogeneous

population of neural cells which included neurons, astrocytes and oligodendrocytes based on the expression of neural specific markers (genes

and proteins) and also neurotransmitters such as dopamine, g-aminobutyric

acid and serotonin. This study demonstrates that growth factors can

induce stable populations of neural cells. further, preliminary work has

raised the possibility of obtaining homogeneous subpopulations of neural

cells by using different combinations of these growth factors thereby

providing cell populations suitable for therapeutic use in a variety of

neurodegenerative diseases. Work is in progress to optimize this transdifferentiation process and also to elucidate the underlying mechanism.

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AN 2003:336751 BIOSIS

DN PREV200300336751

TI Heparan Sulfate Oligosaccharides Modulate the Proliferation and Differentiation of Human Multipotent Progenitor Cells.

AU Gupta, Pankaj [Reprint Author]; Pan, Chendong [Reprint Author]; Nelson,

Matthew S. [Reprint Author]; Reyes, Morayma [Reprint Author]

CS Hem/Onc Section, VA Med. Ctr., Minneapolis, MN, USA

SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2054. print.

Meeting Info.: 44th Annual Meeting of the American Society of Hematology.

Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; (Meeting Poster)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 23 Jul 2003

Last Updated on STN: 23 Jul 2003

AB Cell surface and matrix (ECM) heparan sulfate (HS) influences embryogenesis by binding to and modulating the activity of several

cytokines (CK). The biological activity of FGF-2, critical for neurogenesis and angiogenesis, requires the formation of a signaling

complex of FGF-2, FGF receptor (FGFR) and cell surface HS (FGF-FGFR-HS).

Our group has shown that specific CK induce in vitro differentiation of

multipotent adult progenitor cells (MAPC) into mesodermal, endodermal and neuro-ectodermal lineages (Reyes M. Blood 98:2615, 2001;

Jiang Y. Nature 418:41, 2002). When cultured with FGF-2, MAPC acquire a neuronal and glial phenotype. MAPC thus provide a powerful model for studying the effect of ECM components like HS, on CK

signaling and stem cell growth and differentiation. We used this model to

examine if and how FGF-2-HS interactions influence MAPC proliferation and neuronal differentiation. Further, to determine if and

how abnormal HS perturb stem cell proliferation and differentiation, we

compared MAPC from patients with Hurler syndrome, an inborn metabolic error with accumulation of structurally abnormal HS and progressive neurological dysfunction. HS from normal MAPC bound avidly to FGF-2 (Kd 69 nM). In contrast, subpopulations of Hurler HS

either bound to FGF-2 with abnormally low affinity (Kd 125 nM), or failed

to bind at all. Consistent with this abnormality, the binding of <sup>125</sup>I-FGF-2 to Hurler MAPC (in the FGF-FGFR-HS complex) was 55% of that to normal MAPC. Hurler HS reduced the binding of <sup>125</sup>I-FGF-2 to normal MAPC by 50%, indicating that these abnormal HS interfere with FGF-2 binding in the FGF-FGFR-HS complex.

Enzymatic removal of Hurler cell surface HS, followed by addition of

normal HS, doubled the <sup>125</sup>I-FGF-2 binding to Hurler MAPC. We next compared the biological effect of the interactions between FGF-2 and

normal HS vs Hurler HS. FGF-2 mediated proliferation of normal MAPC required normal HS, as it was completely abrogated by enzymatic removal of cell surface HS and completely restored by addition

of normal HS, but not by addition of Hurler HS. In contrast, Hurler

MAPC failed to proliferate in presence of FGF-2. Further, Hurler HS markedly impaired FGF-2 mediated proliferation of normal MAPC

. Enzymatic removal of the interfering cell surface HS from Hurler

MAPC, followed by addition of normal HS, restored FGF-2 responsiveness. We also examined if MAPC HS induces FGF-2 signaling in HS-deficient target cells (FGFR1 transfected F32 cells that

depend on exogenous HS). FGF-2 induced proliferation of F32 cells was

significantly greater in presence of normal HS compared to Hurler HS.

Finally, while normal MAPC acquired the immunophenotype of neuronal cells, astrocytes and oligodendrocytes when cultured with FGF-2,

Hurler MAPC failed to differentiate into cells with a neuronal immunophenotype under the same conditions, and instead generated astrocytic and oligodendrocytic cells. Commitment of Hurler MAPC to the neuronal lineage (but not glial lineage) was blocked at an early

stage of differentiation, consistent with defective FGF-2 signaling

mediated by abnormal HS. These studies indicate that (i) HS is critical

for CK-mediated proliferation and differentiation of progenitor cells (ii)

in presence of the same CK, the differentiation pathway followed by a

progenitor cell may depend on the type of HS present, and most importantly, that (iii) normal HS can restore CK signaling and biological

response in progenitor cells in diseases with abnormal HS.

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FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:59:20 ON 20 APR 2009  
L1 348 S MULTIPOTENT ADULT STEM CELL OR MAPC  
L2 3 S L1 AND HOMOLOGOUS RECOMBIN?  
L3 2 DUP REM L2 (1 DUPLICATE REMOVED)  
L4 24 S L1 AND REVIEW  
L5 17 DUP REM L4 (7 DUPLICATES REMOVED)

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L6 0 S L1 AND PY,=2002

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:09:37 ON 20 APR 2009  
L7 135 S L1 AND PY<=2002  
L8 88 DUP REM L7 (47 DUPLICATES REMOVED)  
L9 0 S L8 AND VECTOR  
L10 0 S L8 AND RECOMBIN?

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L8 ANSWER 11 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson  
Corporation on  
STN  
AN 2003:336753 BIOSIS  
DN PREV200300336753  
TI Formation of Multinucleated Myotubes from Human Multipotent Adult  
Proenitor Cells.  
AU Muguruma, Yukari [Reprint Author]; Nakamura, Yoshihiko [Reprint  
Author];  
Yahata, Takashi [Reprint Author]; Ando, Kiyoshi [Reprint  
Author]; Kato,  
Shun-ich [Reprint Author]; Hotta, Tomomitsu [Reprint Author]  
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School of

Medicine, Kanagawa, Japan

SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2056. print.

Meeting Info.: 44th Annual Meeting of the American Society of Hematology.

Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

Conference; (Meeting Poster)

LA English

ED Entered STN: 23 Jul 2003

Last Updated on STN: 23 Jul 2003

AB Recent studies have shown that multipotent adult progenitor cells (MAPC) derived from post-natal bone marrow can differentiate into osteoblasts, chondrocytes, adipocytes as well as endothelial cells and hepatocyte-like cells. Several studies also reported myotubes can be derived from bone marrow cells; however, in their system treatment with demethylation drugs, known mutagen such as 5 azacytidine, seems to be essential for inducing myotube formation, which hinders from therapeutic use. We here demonstrate the derivation of multinucleated myotubes from human adult bone marrow MAPC using clinically applicable culture condition. Frozen (n=20) and fresh (n=3) bone marrow cells were used as a source of MAPCs. MAPCs were established according to the published method (Blood, 2001). Briefly, fresh bone marrow cells were negatively selected for CD45-/GryA- cells before plating, and emerging adherent cells were expanded. On the other hand, frozen cells were plated as mononuclear cells and cultured for 2apprx3 weeks, and then CD45-/GryA- cells were selected. Adherent cells growing in both cultures were maintained at 500apprx3000 cells/cm2 and routinely expanded more than 25 population doublings before using for the study. Cytogenetic analysis detected no abnormality. To induce multinucleated myotube formation, cells were transferred to medium containing 5% FCS, bFGF, VEGF and IGF-1, and allowed

to become confluent. Differentiation was confirmed by the expression of myogenic markers using RT-PCR and immunocytochemical staining. A time course analysis revealed the presence of scattered MyoD and myogenin positive mononuclear cells by day 7. It appeared that in situ proliferation of those cells led to the formation of myotubes. Around day 10, numerous multinucleated tubes, which were positive for alpha-actinin and skeletal myosin, were evident. Typical striated muscle ultrastructure was demonstrated in electron microscopy. Addition of BMP4 in the culture appeared to facilitate cell proliferation and/or cell fusion, resulting in the increased number of nuclei in myotubes as well as number of myotubes formed in the culture. At day 14, mononuclear cells that were positive for MyoD and myogenin remained in the culture, indicative of heterogeneity in cell maturation in our culture system and continuous new myotube formation. All in all, we have successfully induced multinucleated myotubes from adult bone marrow MAPC in vitro, which will be useful in treatment or improvement of life quality in patients with muscular disorders. To assess the engraftment and differentiation of MAPC derived muscle cells in vivo, eGFP-transduced MAPC with or without myogenic induction were injected into tibialis anterior muscles of NOD/SCID mice. The result of in vivo study is currently under analysis.

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AN 2003:336377 BIOSIS

DN PREV200300336377

TI Ex Vivo Differentiation of Mouse Multipotent Adult Progenitor Cells

(mMAPC) into Functional Dopaminergic Neurons.

AU Jiang, Yuehua [Reprint Author]; Henderson, Dori [Reprint Author]; Blackstedt, Mark [Reprint Author]; Chen, Angel [Reprint Author]; Lisberg,

Aaron [Reprint Author]; Miller, Robert F. [Reprint Author]; Verfaillie,



Catherine M. [Reprint Author]  
 CS Stem Cell Institute and Department of Medicine, University of Minnesota,  
 Minneapolis, MN, USA  
 SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 95.  
 print.  
 Meeting Info.: 44th Annual Meeting of the American Society of Hematology.  
 Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.  
 CODEN: BLOOAW. ISSN: 0006-4971.  
 DT Conference; (Meeting)  
 Conference; (Meeting Poster)  
 Conference; Abstract; (Meeting Abstract)  
 LA English  
 ED Entered STN: 23 Jul 2003  
 Last Updated on STN: 23 Jul 2003  
 AB Recently we reported that a rare cell, termed Multipotent Adult Progenitor  
 Cells or MAPC, within mouse bone marrow mesenchymal stem cell cultures can be expanded without obvious senescence,  
 differentiate in  
 vitro to cells of the three germ layers, and contribute to most somatic  
 tissues when injected into an early blastocyst. Here we demonstrate that  
 mMAPC can differentiate to functional dopaminergic neurons in vitro.  
 MAPC were cultured in FN-coated wells in serum-free medium without  
 EGF, PDGF, LIF (cytokines required for maintenance of MAPC) sequentially for 7 days with 100ng/ml bFGF in serum-free medium, followed  
 by 7 days with 10ng/ml FGF-8 plus 100ng/ml Sonic Hedgehog (SHH), followed  
 by 10 ng/ml BDNF in N2 medium. On day 21, MAPC-progeny was co-cultured with murine fetal astrocytes in N2 medium for an additional 7  
 days. Quantitative RT-PCR was used to detect expression of neuroectodermal genes. Levels of Otx2 mRNA increased more than 50-fold by  
 day 2 and became maximal by day5. On day 4, Otx1 mRNA was upregulated 3  
 to 5-fold, and on day 5 levels of Pax2, Pax5 and nestin mRNA increased 400  
 to 800-fold over undifferentiated MAPC. On day 11 levels of Nurrl increased 600-fold over undifferentiated mMAPC and TH mRNA was  
 detectable. On day 14, cells staining positive for glial fibrillary  
 acidic protein (GFAP/astrocytes; 25%), myelin basic protein (MBP/oligodendrocytes; 25%) and neurofilament-200 (NF200 neurons; 50%)

could be detected. On day 21, neurons acquired a more mature phenotype, demonstrating polarization, and expression of neurotransmitters (GABA, dopamine and serotonin). However, electrophysiological studies did not demonstrate presence of voltage-gated sodium-channels. After 28 days of sequential treatment of cytokines and co-culture with astrocytes, neurons matured further. Immunofluorescence microscopy showed that 20-30% of cells were dopadecarboxylase (DDC) and tyrosine hydroxylase (TH) positive, 20-30% tryptophan hydroxylase (TrH) positive and 50-60% GABA positive.<sup>14</sup> mature-neuron-like cells were chosen for patch clamp evaluation of current and voltage clamp recordings. In 10/14 cells sodium currents and spiking could be evoked. Of them current injection evoked repetitive spiking in 4 of the cells and single spiking in 6 cells. Voltage-clamp recordings from the spiking cells demonstrated the presence of tetrodotoxin-sensitive inward currents, indicating that currents were mediated by voltage-gated sodium channels. These data demonstrated therefore that MAPC can differentiate in vitro to functional dopaminergic neurons.

As MAPC can be purified and expanded from marrow, they may constitute a useful source to treat Parkinson disease. In vivo study is currently going on.

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 STN  
 AN 2003:337272 BIOSIS  
 DN PREV200300337272  
 TI Efficient Transfection of Human CD34+ Cells with "Sleeping Beauty" DS-RED Transposons.  
 AU Lamming, Christopher E. [Reprint Author]; Converse, Andrea [Reprint Author]; Augustine, Lance [Reprint Author]; McIvor, R. Scott [Reprint Author]; Verfaillie, Catherine M. [Reprint Author]  
 CS Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA

SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2574. print.  
Meeting Info.: 44th Annual Meeting of the American Society of Hematology.  
Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 23 Jul 2003  
Last Updated on STN: 23 Jul 2003

AB The promise of hematopoietic stem cell (HSC) gene therapy has been limited  
by low viral transduction efficiencies of HSC and potential dangers of  
using viral agents in a clinical setting. Non-viral gene therapy is a  
safer alternative to viral based systems. The transposon plasmid based  
system has been successfully used to stably introduce non-viral DNA into  
hematopoietic cell lines. However, CD34+ stem cells remain difficult to  
target as shown by NOD-SCID repopulation assays of transfected cells  
(Hossle J.P., 2002). We tested whether CD34+ cells could be stably  
transfected with DS-RED expressing transposons. DS-RED plasmids were  
constructed with or without transposase with CMV or CAGGS promoters  
driving DS-RED expression. Plasmid size was 11-15 Kb, depending on the  
presence of transposase. 60µg/mL plasmid DNA was either electroporated or  
nucleoporated. Electroporation conditions were: 250v, 1600µF in a 0.5ml  
cuvette. Nucleoporation conditions were CD34+ nucleoporation media and  
machine setting U08. 2x10<sup>5</sup>-2x10<sup>6</sup> cord blood CD34+ cells were electroporated in media containing X-VIVO 10, 5% FCS, 20 ng/ml SCF,  
Flt-3L, IL7 and TEPO at 250v, 1600µF. After nucleoporation or electroporation, cells were pelleted and incubated at 37°C for 15min  
before transfer to transwells over AFT024 stroma in media containing  
RPMI1640, 20% FCS and cytokines as above. 72 hours later, cells were  
harvested, stained with Annexin V and 7AAD, and live DS-RED positive cells

selected by FACS. 20-40% of electroporated and 10-35% of nucleoporated

CD34+ samples were DS-RED positive. However, Annexin V and 7AAD staining

showed that most transfected cells were undergoing apoptosis. Only

2.5+-0.3% of electroporated and 2%+-0.6% of nucleoporated CD34+ cells were

Annexin V-7AAD-DS-RED+, which were then deposited on AFT024 feeders at 10

cells/well. Wells were scored 1, 2 and 3 weeks later for DS-RED+ cells.

After 1 week, 80+-5% of electroporated or nucleoporated CD34+ progeny were

positive, and after 2 and 3 weeks, 67+-6% were DS-RED positive.

Confirmation of DNA integration using PCR is underway.

Likewise, studies

are underway to demonstrate that CD34+ cells still retain CFC activity.

We are also investigating the possibility of using this method to introduce DS-RED plasmids into a rare population of stem cells, recently

identified in our laboratory in human and rodent marrow, termed multi-potent adult progenitor cells, or MAPC, that may be an attractive alternative for gene therapy as they can contribute up to 10%

of the hematopoietic system following transplantation into a minimally

irradiated recipient. We have shown higher rates of transfection (4.8+-0.6%) and long term expression of DS-RED in MAPC by fluorescence (78+-8% at 4 weeks) but have not yet shown definitive differentiation ability of DS-RED expressing progeny to mesodermal,

endodermal and ectodermal lineages. In conclusion although low rates of

transfection are seen, Transposon-based non-viral vectors hold promise for

hematopoietic stem cell gene therapy. In addition MAPC, that can likewise be transfected with the Transposon system, may prove to be an

attractive target for clinical transplantation due to the ability to

expand transfected MAPC long-term without loss of engraftment and multi-lineage differentiation ability.

L8 ANSWER 14 OF 88 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights

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AN 2002201327 EMBASE

TI Embryonic stem cell research: The relevance of ethics in the progress of science.

AU Ruiz-Canela, Miguel (correspondence)  
 CS Department of Biomedical Humanities, University of Navarra,  
 Apartado 177,  
 E-31080 Pamplona, Spain. mcanela@unav.es  
 SO Medical Science Monitor, (2002) Vol. 8, No. 5, pp. SR21-SR26.  
 Refs: 50  
 ISSN: 1234-1010 CODEN: MSMOFR  
 CY Poland  
 DT Journal; Article  
 FS 017 Public Health, Social Medicine and Epidemiology  
 029 Clinical and Experimental Biochemistry  
 LA English  
 SL English  
 ED Entered STN: 27 Jun 2002  
 Last Updated on STN: 27 Jun 2002  
 AB Experimentation with embryonic stem (ES) cells has become an  
 important  
 breakthrough in medical research. However, it is also a source  
 of  
 controversy, because it requires the destruction of the human  
 embryos used  
 to derive ES cells. This paper deals with some of the ethical  
 issues  
 concerning ES cell research. To begin with, the terms used in  
 the debate  
 on the ethical status of the human embryo need to be defined.  
 Apart from  
 the presumed benefits of ES cell research, we should also  
 consider such  
 issues as the strong opposition to this research by a large part  
 of  
 society, who argue in favour of protecting and respecting human  
 embryos;  
 the fragility and defenseless of human embryos; and the  
 contradiction in  
 terms inherent in the statement that human embryos must be  
 treated with  
 respect. Secondly, we should focus on possible conflicts  
 between the  
 financial, scientific, and ethical aspects of this debate.  
 Thirdly, the  
 significance of social and political debate requires clear and  
 complete  
 information that takes all consequences into account. Finally,  
 the paper  
 suggests how multipotent adult stem  
 cell research may be an optimal and realistic alternative to ES  
 cell research.

L8 ANSWER 15 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN  
 AN 2002:642936 CAPLUS  
 DN 137:349940

TI Purification, characterization and differentiation of multipotent  
 adult stem cell from post-natal human bone  
 marrow  
 AU Reyes, Morayma Gil  
 CS Univ. of Minnesota, Minneapolis, MN, USA  
 SO (2001) 202 pp. Avail.: UMI, Order No. DA3029106  
 From: Diss. Abstr. Int., B 2002, 62(10), 4322  
 DT Dissertation  
 LA English  
 AB Unavailable

L8 ANSWER 16 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN  
 AN 2001:115268 CAPLUS  
 DN 134:159887  
 TI Multipotent adult stem cells and methods for isolation  
 IN Furcht, Leo T.; Verfaillie, Catherine M.; Reyes, Morayma  
 PA USA  
 SO PCT Int. Appl., 132 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.
WO 2001011011	A2	20010215	WO 2000-US21387
WO 2001011011	A3	20010510	
WO 2001011011	A9	20020725	
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2381292	A1	20010215	CA 2000-2381292
AU 2000066218	A	20010305	AU 2000-66218
AU 784163	B2	20060216	
EP 1226233	A2	20020731	EP 2000-953840

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,  
MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL  
JP 2003506075 T 20030218 JP 2001-515800  
20000804  
NZ 517002 A 20040625 NZ 2000-517002  
20000804  
ZA 2002001125 A 20040510 ZA 2002-1125  
20020208  
IN 2002CN00311 A 20070223 IN 2002-CN311  
20020228  
US 20050181502 A1 20050818 US 2005-84256  
20050321  
US 20060008450 A1 20060112 US 2005-151689  
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US 20060030041 A1 20060209 US 2005-238234  
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US 20060263337 A1 20061123 US 2005-269736  
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AU 2006202072 A1 20060615 AU 2006-202072  
20060516  
US 20070009500 A1 20070111 US 2006-446560  
20060602  
JP 2008044965 A 20080228 JP 2007-273194  
20071019  
IN 2008CN02360 A 20090306 IN 2008-CN2360  
20080512  
PRAI US 1999-147324P P 19990805  
US 1999-164650P P 19991110  
AU 2000-66218 A 20000804  
JP 2001-515800 A3 20000804  
WO 2000-US21387 W 20000804  
US 2001-268786P P 20010214  
US 2001-269062P P 20010215  
US 2001-310625P P 20010807  
US 2001-343836P P 20011025  
WO 2002-US4652 W 20020214  
IN 2002-CN311 A3 20020228  
US 2002-48757 A1 20020821  
US 2003-527249P P 20031204  
US 2004-467963 A2 20040105  
US 2004-963444 B2 20041011  
WO 2004-US40932 A1 20041206  
US 2005-84256 A2 20050321  
US 2005-151689 A2 20050613

AB The invention provides isolated stem cells of non-embryonic  
origin that

can be maintained in culture in the undifferentiated state or  
differentiated to form cells of multiple tissue types. Also  
provided are

methods of isolation and culture, as well as therapeutic uses  
for the

isolated cells. Multipotent adult stem cells were obtained from bone marrow mononuclear cells of humans and mice by depletion of CD45-pos. and glycophorin A-pos. cells with microbeads. Conditions are described for culturing the cells and for differentiating them into many kinds of cells.

RE.CNT 8            THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8    ANSWER 17 OF 88    CAPLUS    COPYRIGHT 2009 ACS on STN  
AN    2001:68346    CAPLUS  
TI    Method of reducing turbo lag in diesel engines having exhaust gas recirculation  
IN    Kolmanovsky, Ilya V.; Van Nieuwstadt, Michiel J.; Moraal, Paul Eduard  
PA    Ford Motor Company, USA  
SO    U.S., 10 pp.  
      CODEN: USXXAM  
DT    Patent  
LA    English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.
DATE	-----	----	-----	-----
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PI	US 6178749	B1	20010130	US 1999-237737
	19990126 <--			
PRAI	US 1999-237737		19990126	
AB	A method of reducing turbo lag in a compression ignition engine having an exhaust gas recirculation system (EGR) and a variable geometry turbocharger (VGT). The method includes the steps of determining an intake manifold pressure and intake manifold mass airflow setpoint, MAPd and MAFd, as a function of the current engine speed and requested fueling rate (Wf,REQ). The method further includes modifying the setpoints by a transient governor to generate modified setpoints, MAFc and MAPc, as a function of MAFd and MAPd, resp., and feeding the modified setpoints to the controller to drive the turbocharger and EGR valve to the desired setpoints, thereby maximizing the amount of fresh air admitted to the engine during transient operation. Another embodiment of the method for reducing turbo lag coordinates the controller gains between the EGR and VGT. The method speeds up the MAF response by using multivariable			



control of both the EGR and VGT to aggressively regulate airflow to the desired setpoint.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson  
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STN

AN 2002:261590 BIOSIS

DN PREV200200261590

TI Microarray analysis of differentiation from MAPC to osteoblasts.

AU Qi, Huilin [Reprint author]; Aguiar, Dean [Reprint author];  
Verfaillie,

Catherine [Reprint author]

CS Medicine, Stem Cell Institute, University of Minnesota,  
Minneapolis, MN,

USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 832a.  
print.

Meeting Info.: 43rd Annual Meeting of the American Society of  
Hematology,

Part 1. Orlando, Florida, USA. December 07-11, 2001. American  
Society of

Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 1 May 2002

Last Updated on STN: 1 May 2002

AB Human bone marrow derived multipotent adult progenitor cells (MAPC

) differentiate into osteoblasts, chondrocytes, adipocytes,  
myocytes,

endothelial cells and neuronal cells. In order to identify  
genes involved

in commitment of MAPC to osteoblasts, we examined differentially  
expressed genes by microarray analysis in MAPC and MAPC  
treated with beta-glycerophosphate, Dexamethasone and ascorbic  
acid to

induce the osteoblast phenotype. Total RNA from MAPC isolated  
from three donors and MAPC induced to osteoblast cell lineage at  
days 1, 2 and 7 were hybridized to microarrays from Research

Genetics

(4324 human genes). We found that 157 genes are up regulated  
(gtoreq2

fold), 212 genes are down regulated (gtoreq2 fold) in day 1  
differentiated

cells. 310 genes are up and 432 are down regulated by day 2; and  
787 up

and 358 down regulated by day 7. Three transcription factors  
were up

regulated at all three time points: DGS1, which belongs to TBX family and known to have a possible role in osteogenesis, DSIPI and BRCA-1. Some transcription factors were up regulated only on day 1, such as CLIM1, and some were only up regulated on day 2, such as AP-4, USF2, HOXA5, and HOX11. HOX11 is known to play a role in osteogenesis and chondrogenesis. The transcription factors HEMX1, Sox22, short stature homeobox 2 and cbfa3 were up regulated on both days 2 and 7, MSX2, Sox3, Sox4, MEF2b, MEF2D, NFIC and NFIX were among transcription factors up regulated on day 7. MSX2 is required for induction of CbFal, the master transcription factor for osteoblast differentiation, which did not become up regulated until day 7 (detected by microarray analysis and Real Time RT-PCR) and 14 (detected by Real Time RT-PCR). Thirty-seven transcription factors were down regulated during differentiation, including ID3, CA150, Zinc finger proteins 6 and 162, and early growth response 1 which were suppressed at all three time points (days 1, 2, and 7) examined. CITED2 was down regulated at day 2. FUSE1 known to be more active in undifferentiated cells was down regulated at both days 2 and 7. The transcriptional repressor ZF87/MAZ, a known inhibitor of the parathyroid hormone receptor (a critical receptor in osteogenesis) gene expression, was suppressed by day 7 of MAPC differentiation to the osteoblast phenotype. Using Real Time RT-PCR we have confirmed differential expression of >20 genes as detected by microarray analysis. As up-regulation of cbfal was only seen after 7-14 days, microarray analysis of differentiation of MAPC to the osteoblast lineage and other lineages should provide important new insights in the pivotal molecular events required for osteoblast and other differentiation.

STN

AN 2002:261548 BIOSIS

DN PREV200200261548

TI Origin of endothelial progenitors in human post-natal bone marrow.

AU Reyes, Morayma [Reprint author]; Dudek, Arek; Jahagirdar, Balkrishna;  
Koodie, Lisa; Verfaillie, Catherine

CS Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 821a. print.  
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,  
Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 1 May 2002  
Last Updated on STN: 1 May 2002

AB Until recent, it was thought that blood vessel formation in post-natal life was mediated by sprouting of endothelial cells from existing vessels.  
However, recent studies have suggested that endothelial "stem cells" may persist into adult life, where they contribute to the formation of new blood vessels, suggesting that like during development neoangiogenesis in the adult may at least in part depend on a process of vasculogenesis.  
Precursors for endothelial cells have been isolated from BM and peripheral blood. The ontogeny of these endothelial progenitors is unknown. We have previously described a rare cell in human post-natal bone marrow capable of differentiating not only in mesenchymal cell types, but also cells of neuroectodermal origin, termed multipotent adult progenitor cell or MAPC. We here show that these CD34-, vascular-endothelial (VE)-cadherin-, AC133+ and fetal liver kinase (Flk1)+ MAPC that co-purifies with mesenchymal stem cells is a progenitor for the angioblasts. In vitro, MAPC cultured for 3 days with vascular endothelial growth factor (VEGF) differentiated into CD34+, VE-cadherin+, Flk1+ cells, a phenotype consistent with angioblasts. Subsequently,

MAPC differentiated into cells that express mature endothelial markers, such as vWF, Muc-18, CD36, CD31, CD62-P, Tie and Tek. In vitro generated endothelial cells from MAPC functioned as mature endothelial cells, as they (A) could uptake LDL; (B) secreted vWF and widened gap junctions under histamine exposure; (C) reacted to inflammatory cytokines (IL-1a) by upregulating HLA-Class I/II and VCAM, CD62P/E; (D) upregulated VEGF secretion and VEGFR expression under hypoxia and; (E) formed vascular tubes when plated on ECM. When infused in vivo, endothelial cells generated in vitro from MAPC contributed approximately 40% to neoangiogenesis in the setting of tumor angiogenesis and wound healing. Moreover, undifferentiated MAPC infused in NOD-SCID mice differentiated in vivo in response to local cues in tumors into endothelial cells that contribute to tumor neoangiogenesis. This in vitro model of pre-angioblast to endothelium differentiation should prove very useful to study commitment to the angioblast stage and beyond. Because MAPC can be culture expanded without obvious senescence for >80 population doublings, they may be an important source of endothelial cells for cellular pro- or anti-angiogenic therapies.

L8 ANSWER 20 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on  
STN  
AN 2002:261451 BIOSIS  
DN PREV200200261451  
TI Functional abnormalities in heparan sulfate in Hurler syndrome are  
associated with defective differentiation of multipotent adult progenitor cells.  
AU Gupta, Pankaj [Reprint author]; Reyes, Morayma; Verfaillie, Catherine M.;  
Nelson, Matthew S. [Reprint author]  
CS Medicine/Hem-Onc, VA Med. Center, Minneapolis, MN, USA  
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 797a. print.  
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,  
Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.  
DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 1 May 2002

Last Updated on STN: 1 May 2002

AB Hurler syndrome (mucopolysaccharidosis type I) is an inborn error of

metabolism in which absence of a degradative enzyme leads to progressive

tissue accumulation of heparan and dermatan sulfates (HS, DS).

How these

incompletely digested HS and DS cause abnormalities in the development and

functioning of diverse tissues is unclear. It is known that HS directly

influence normal tissue morphogenesis by binding to and modulating the

activity of several proteins involved in signaling and developmental

patterning. FGF-2, which plays a critical role in neuronal development,

angiogenesis and hematopoiesis, is one such protein dependent on specific

interactions with HS for biological activity. Thus far, the inability to

obtain primary Hurler cells that are representative of cell types in

diverse tissues and can be expanded easily in vitro, has been a major

limitation to performing functional studies on HS in Hurler syndrome. We

hypothesized that the abnormal size and sulfation of Hurler HS leads to

aberrant functional properties (affinity for binding critical cytokines),

which contribute to abnormalities in developing tissues (e.g., neurons).

We examined the structure and function of HS purified from multipotent

adult progenitor cells (MAPC) that we have identified and cultured from Hurler and normal BM. Normal MAPC can differentiate in vitro into mesodermal, endodermal and ectodermal lineages, including neuronal and glial cells. We found that the structure

of HS accumulated in the extracellular matrix (ECM) of Hurler MAPC

is markedly abnormal. HS molecules from Hurler cells were small (5 kD vs

42 kD), highly sulfated (65% vs 22% sulfation of total HS), and had

abnormal oligosaccharide domains, compared to HS from normal MAPC . To determine if structural abnormalities identified in Hurler

HS result

in abnormal function, we examined the binding of HS from the ECM of normal and Hurler MAPC to FGF-2. HS from normal MAPC bound to FGF-2 as a homogenous population (Kd 69 nM). In contrast, in Hurler HS, 3 subpopulations were identified with markedly different affinities: (i) the major subpopulation of Hurler HS bound with abnormally low affinity (Kd 125 nM), (ii) a second subpopulation of HS failed to bind altogether, and (iii) only the smallest (minor) subpopulation bound with normal affinity (Kd 74 nM) to FGF-2. Hurler HS also bound abnormally to SDF-1alpha and SDF-1beta, chemokines that are required for stem cell homing and migration and for cerebellar development. These data indicate that structurally abnormal HS deposited in the ECM of Hurler cells has abnormal cytokine binding properties. Finally, we examined if the abnormal interactions between Hurler HS and FGF-2 impair the biological activity of FGF-2. Whereas normal MAPC consistently differentiated into neuronal cells, astrocytes and oligodendrocytes when cultured in presence of FGF-2, Hurler MAPC failed to differentiate into neuronal cells under the same conditions, and only generated astrocytes and oligodendrocytes. Our studies thus identify for the first time a mechanism by which accumulated HS contribute to the developmental pathophysiology of Hurler syndrome (and likely other mucopolysaccharidoses), by perturbing critical HS-protein interactions. These studies also strengthen the rationale for a therapeutic trial of normal/gene corrected MAPC, which can directly differentiate into neuronal and other cell types.

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.49	157.02
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
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(FILE 'HOME' ENTERED AT 14:59:11 ON 20 APR 2009)

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:59:20 ON 20 APR 2009

L1	348 S MULTIPOTENT ADULT STEM CELL OR MAPC
L2	3 S L1 AND HOMOLOGOUS RECOMBIN?
L3	2 DUP REM L2 (1 DUPLICATE REMOVED)
L4	24 S L1 AND REVIEW
L5	17 DUP REM L4 (7 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 15:04:20 ON 20 APR 2009

L6	0 S L1 AND PY,=2002
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FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:09:37 ON 20 APR 2009

L7	135 S L1 AND PY<=2002
L8	88 DUP REM L7 (47 DUPLICATES REMOVED)
L9	0 S L8 AND VECTOR
L10	0 S L8 AND RECOMBIN?

FILE 'STNGUIDE' ENTERED AT 15:13:42 ON 20 APR 2009

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:29:02 ON 20 APR 2009

FILE 'STNGUIDE' ENTERED AT 15:31:51 ON 20 APR 2009

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:36:18 ON 20 APR 2009

=> d bib abs 18 21-50

L8 ANSWER 21 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson  
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STN

AN 2002:261423 BIOSIS

DN PREV200200261423

TI Pluripotent nature of cells in adult marrow copurifying with  
mesenchymal  
stem cells.

AU Jiang, Yuehua [Reprint author]; Jahagirdar, Balkrishna [Reprint  
author];

Largaespada, David [Reprint author]; Reyes, Moryama [Reprint  
author];

Lisberg, Aaron [Reprint author]; Verfaillie, Catherine M.  
[Reprint author]

CS Medicine and Laboratory Medicine, Stem Cell Institute,  
University of

Minnesota, Minneapolis, MN, USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 791a.  
print.

Meeting Info.: 43rd Annual Meeting of the American Society of  
Hematology,

Part 1. Orlando, Florida, USA. December 07-11, 2001. American  
Society of  
Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 1 May 2002

Last Updated on STN: 20 May 2002

AB A number of recent studies have suggested that adult stem cells  
from a

number of tissues may have greater differentiation potential than  
previously thought. We have identified multipotent adult  
progenitor cells

or MAPC, which are co-purified with mesenchymal stem cells and  
have the ability to differentiate in vitro into most mesodermal  
cell types

as well as cells with neuroectodermal and endodermal features  
(See Jiang

et al). In this study, we tested whether MAPC can differentiate  
into functional cells of all tissues in vivo, by injecting them  
in early



blastocysts. MAPC were generated from marrow of beta-galactosidase (beta-gal) transgenic ROSA26 mice. One or 10-12 ROSA26 MAPC were microinjected into 116 and 38 early blastocysts, resp. Blastocysts were transferred to foster mothers, the mice were allowed to develop, and then 7 litters were born. The number of mice per litter varied from 1 to 8, for a total of 35 mice. Animals born from microinjected blastocysts were of similar size as normal animals and did not display any overt anatomical abnormalities. All of the mice derived from blastocysts in which 10-12 MAPC had been injected and 50% of the mice derived from blastocysts microinjected with 1 MAPC had >1% of cells in the tail that contained the NEO transgene compared to ROSA26 mice from which MAPC were derived. MAPC contributed to all tissues, including the central nervous system, skeletal muscle, cardiac muscle, liver, intestine, lung, kidney, spleen, marrow, blood, and skin as shown by X-GAL staining and staining with an anti-beta-gal-FITC antibody. beta-gal+ cells expressed markers typical for the tissue in which they incorporated. Co-labeling was seen for beta-gal, cardiac troponin-I and dystrophin in the heart, and beta-gal and skeletal actin or dystrophin in the skeletal muscle. Co-staining for beta-gal, albumin and anti-cytokeratin (CK)-18 was seen in the liver and pan-CK and beta-gal in the intestine and skin. beta-gal+ cells in the kidney co-stained with vimentin (glomeruli) or pan-CK (tubuli). Cells in spleen, bone marrow and blood showed co-labeling with anti-beta-gal and anti-CD45, anti-CD19, anti-CD3, anti-Gr1 and anti-Mac1 antibodies. In the central nervous system, we saw co-labeling of cells for beta-gal and NF200, GFAP, and MBP. As all animals had normal organs function, MAPC differentiate in vivo into functional cells of the three germ layers. Similar results were seen for animals derived from blastocysts in which 1 or 10-12 MAPC had been injected, indicating that chimerism following blastocyst injection occurs from a single MAPC. Together with the data presented elsewhere from our group showing that MAPC engraft and differentiate in vivo when transplanted

postnatally in uninjured animals (Jahagirdar et al), results reported here  
prove the notion that adult stem cells have significantly greater differentiation potential than previously thought, and that some adult stem cells are pluripotent.

L8 ANSWER 22 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on  
STN

AN 2002:261424 BIOSIS

DN PREV200200261424

TI Multipotent adult progenitor cells from bone marrow differentiate into  
urea producing hepatocyte-like cells.

AU Schwartz, Robert E. [Reprint author]; Jiang, Yuehua [Reprint author];

Blackstad, Mark [Reprint author]; Reyes, Moryama [Reprint author];

Verfaillie, Catherine M. [Reprint author]

CS Medicine, Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 791a. print.

Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,

Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 1 May 2002

Last Updated on STN: 1 May 2002

AB We have identified a population of primitive cells in normal human, mouse

and rat post natal bone marrow that we have termed Multipotent Adult

Progenitor Cell or MAPC that have multipotential differentiation and extensive proliferation potential. MAPC differentiate in vitro into most mesodermal and neuroectodermal lineages and in vivo into

all embryological lineages (see abstracts Jiang et al). Several groups

have demonstrated that hepatocytes and cholangiocytes can be derived from

bone marrow in vivo. We investigated whether rat MAPC can differentiate into hepatocytes in vitro. MAPC were initially plated at 19,000 cells/cm<sup>2</sup> on fibronectin coated plates and chamber slides

with 2% FCS containing medium supplemented with EGF, PDGF and LIF, medium used to expand MAPC. After one day, MAPC expansion media was removed and a serum free media with the sole cytokines 10 ng/mL FGF-4 and 10 ng/mL HGF was added. Cultures were evaluated 2, 4, 7, 10, 14, 17, 20, and 24 days after culture conditions were switched. Morphology of the cells changed during the experiment from initially a spindle, thin shaped cell to a cuboidal, large cell. PAS staining at day 14 demonstrated positive granules similar to that of hepatocytes. Immunohistochemistry demonstrated that cells stained positive for cytokeratin (CK)-8 and CK18, HNF-3beta, HNF-4, HNF-1, GATA-4, and albumin with increasing numbers of cell staining at later time points. By day 24, approximately 40% of cells stained positive for albumin and CK18. Not all of these markers are specific for hepatocytes, however taken together they strongly suggest commitment of these cells towards the hepatocyte lineage. Quantitative PCR demonstrated a peak of CK19 mRNA expression two days after addition of the differentiation media which decreased to levels seen in MAPC. Likewise, levels of HNF-3beta mRNA increased by day 2, and decreased to level of 5 times higher than in MAPC. We also showed that MAPC induced to differentiate with FGF-4 and HGF produced urea from day 4 which increased to day 14 and leveling off thereafter. The per cell production of urea over time is comparable to urea production by hepatocytes grown in monolayer. We therefore show that MAPC's can differentiate in vitro into urea producing hepatocyte-like cells.

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STN

DUPLICATE 3

AN 2001:493528 BIOSIS

DN PREV200100493528

TI Isolation of multipotent adult stem cells from the dermis of mammalian skin.

AU Toma, Jean G. [Reprint author]; Akhavan, Mahnaz [Reprint author]; Fernandes, Karl J. L. [Reprint author]; Barnabe-Heider, Fanie [Reprint author]; Sadikot, Abbas; Kaplan, David R. [Reprint author]; Miller, Freda

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SO Nature Cell Biology, (September, 2001) Vol. 3, No. 9, pp.  
778-784. print.  
ISSN: 1465-7392.

DT Article

LA English

ED Entered STN: 24 Oct 2001  
Last Updated on STN: 23 Feb 2002

AB We describe here the isolation of stem cells from juvenile and  
adult  
rodent skin. These cells derive from the dermis, and clones of  
individual  
cells can proliferate and differentiate in culture to produce  
neurons,  
glia, smooth muscle cells and adipocytes. Similar precursors  
that produce  
neuron-specific proteins upon differentiation can be isolated  
from adult  
human scalp. Because these cells (termed SKPs for skin-derived  
precursors) generate both neural and mesodermal progeny, we  
propose that  
they represent a novel multipotent adult stem  
cell and suggest that skin may provide an accessible, autologous  
source of stem cells for transplantation.

L8 ANSWER 24 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson  
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AN 2002:250146 BIOSIS

DN PREV200200250146

TI Splinkerette-ligated captured T7 (SCT)/RT-PCR, a new method to  
determine  
retroviral integration flanking sequences.

AU Lund, Troy C. [Reprint author]; Lenvik, Todd [Reprint author];  
Reyes,  
Moryama [Reprint author]; Jiang, Yuehua [Reprint author];  
Verfaillie,  
Catherine M. [Reprint author]

CS Stem Cell Institute, University of Minnesota, Minneapolis, MN,  
USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 745a.  
print.  
Meeting Info.: 43rd Annual Meeting of the American Society of  
Hematology,  
Part 1. Orlando, Florida, USA. December 07-11, 2001. American  
Society of  
Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 24 Apr 2002  
Last Updated on STN: 24 Apr 2002

AB The ability to determine retroviral integration specific sequences is important in determining clonal expansion in bone marrow transplant, cloning, and the generation of virally transduced clonal cell line. In addition, retroviral marking is often used to demonstrate single stem cell derivation of differentiated cells, in vitro and in vivo. There are several methods described, such as inverse-PCR, two-step PCR, and ligation-mediated PCR. We have developed a PCR assay which is both highly specific and highly sensitive to detect integration specific sequences. This method, termed splinkerette-ligated captured T7 RT-PCR, or SCT/RT-PCR, incorporates several key elements to make it both sensitive and specific: a splinkette linker, magnetic capture of target sequences, and exponential replication of potentially rare sequences using a nested T7 promoter. The target PCR products can be directly sequenced to determine integration sequences. We have successfully determined the integration sequences from as little as 30 pg of provirus containing DNA in the background of 30 ng of untransduced DNA representing a 0.1% transduction rate. We have shown, using retrovirally-marked human multipotent adult stem cells (MASCs), the ability to detect and sequence integration sites (see abstracts from Reyes et al, and Jiang et al). Cells were differentiated along the three primitive embryonic layers, endoderm, mesoderm, and ectoderm. Identical retroviral insertion sites were identified using this technique in the differentiated cells to prove clonal origin. This technique offers investigators great leniency in the amount of DNA and target-rarity in the population of cells being studied. While other techniques have shown 1/1000 clonal cells to be identified, to

our knowledge this is the first technique to identify sequences from as little as 30 pg (10 cells) of DNA in a background of 10,000 cells. This method will aid significantly in determining clonality in transplant experiments as well as the generation of clonal cell populations.

L8 ANSWER 25 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2002:220601 BIOSIS

DN PREV200200220601

TI In vitro and in vivo differentiation of single marrow derived multipotent

adult progenitor cell into astrocytes, oligodendrocytes, and functional

dopaminergic, serotonergic or GABA-ergic neurons.

AU Reyes, Morayma [Reprint author]; Verfaillie, Catherine M.; Ortiz, Xilma;

Henderson, Dori; Lenvik, Todd

CS Stem Cell Institute, Minneapolis, MN, USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 714a. print.

Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,

Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 3 Apr 2002

Last Updated on STN: 3 Apr 2002

AB We have recently described a rare marrow derived cell, termed multipotent

adult progenitor cell (MAPC) that can be expanded without obvious senescence ex vivo and can at the single cell level differentiate

to osteoblasts, chondroblasts, skeletal myoblasts and endothelial cells.

We here demonstrate for the first time that single MAPC from human (h) bone marrow can, depending on the cytokines used, differentiate

into oligodendrocytes, astrocytes, and functional, dopaminergic, serotonergic, or gamma-amino-butyric-acid (GABA)-ergic neurons.

Basic-fibroblast growth factor (bFGF) induced hMAPC to differentiate to

oligodendrocytes, astrocytes and immature neurons whereas epidermal growth

factor and fibroblast growth factor-8b induced differentiation of hMAPC to

GABA-ergic, dopaminergic and serotonergic neurons but not glia. By cDNA array, both bFGF-induced and FGF-8b+EGF-induced MAPC expressed many mature neuronal markers such as synaptic proteins and voltage-gated ion channels. Following coculture with the glioblastoma cell line U-87, FGF-8b induced neurons matured further and generated tetrodotoxin-sensitive Na-gated voltage action potentials. We used retroviral marking and PCR analysis for retroviral integration specific sequences to demonstrate that a single MAPC can differentiate not only into endothelial cells, skeletal myoblast, endodermal cells but also astrocytes, oligodendrocytes and neurons, indicating the non-neuronal nature of MAPC. Finally, 1.4X10<sup>4</sup> undifferentiated hMAPC were transplanted in the ventricles of P1-P3 newborn rats, and rats were analyzed 4 or 10 weeks later for presence and differentiation of hMAPC in the brain. At 4 weeks, hMAPC (cell staining positive with an antibody against human nuclei antibody or human nuclear membrane) had migrated into the subventricular zone and differentiated into astrocytes (positive staining for GFAP) and neurons (positive staining for NeuN, MAP-2, and NF-200). After 12 weeks, hMAPC were found in deeper areas of the brain such as hippocampus and striatum. Human cells stained positive for NueN and NF-200. In conclusion, adult marrow derived multipotent progenitor cells that differentiate into mature functional neurons as well as glial cells in vitro and in vivo may constitute an extremely valuable source of cells to treat central nervous system disorders.

L8 ANSWER 26 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on

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AN 2002:220599 BIOSIS

DN PREV200200220599

TI Ex vivo and in vivo primitive hematopoiesis from a non-hematopoietic stem cell.

AU Reyes, Morayma [Reprint author]; Koodie, Lisa; Jahagirdar, Balkrishna;

Verfaillie, Catherine M.  
CS Stem Cell Institute, University of Minnesota, Minneapolis, MN,  
USA  
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 713a.  
print.  
Meeting Info.: 43rd Annual Meeting of the American Society of  
Hematology,  
Part 1. Orlando, Florida, USA. December 07-11, 2001. American  
Society of  
Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 3 Apr 2002  
Last Updated on STN: 3 Apr 2002  
AB Multipotent Adult Stem Cells (MASC) from, human bone marrow (BM)  
differentiate at the single cell level into neuroectodermal,  
endodermal  
and many mesodermal lineages, including endothelial cells.  
Because  
endothelium and blood are very closely related in ontogeny, we  
hypothesized that MASC can differentiate into hematopoietic  
cells. eGFP  
transduced human MASC, that are glycophorin-A (GlyA), CD45 and  
CD34  
negative (n=20), were cocultured with the mouse yolk sac  
mesodermal cell  
line, YSM5, as suspension cell aggregates for 6 days in serum  
free medium  
supplemented with 10 ng/mL bFGF and VEGF. After six days, only  
eGFP+  
cells (MASC progeny) remained and YSM5 cells had died.  
Remaining cells  
were transferred to methylcellulose cultures containing 10%  
fetal calf  
serum supplemented with 10 ng/mL BMP4, VEGF, bFGF, SCF, Flt3L,  
hyper IL6,  
TPO, and EPO for 2 weeks. In these cultures, we detected both  
adherent  
eGFP+ cells and small, round non-adherent cells, which formed  
many  
colonies attached to the adherent cells. The non-adherent and  
adherent  
fractions were collected separately and cultured in 10%FCS  
containing  
medium with 10 ng/mL VEGF and bFGF for 7 days. Adherent cells  
stained  
positive for vWF, formed vascular tubes when plated on ECM, and  
were able  
to uptake a-LDL, indicating their endothelial nature. 5-50% of  
the



non-adherent cells stained positive for human specific GlyA and HLA-class I by flow cytometry. Gly-A+/HLA-class-I+ cells were selected by FACS. On Wright-Giemsa, these cells exhibited the characteristic morphology and staining pattern of primitive erythroblasts. Cells were benzidine+ and human Hb+ by immunoperoxidase. By RT-PCR these cells expressed human specific Hb-e, but not Hb-a. When replated in methylcellulose assay with 20%FCS and EPO, small erythroid colonies were seen after 10 days, and 100% of these colonies stained positive for human specific GlyA and Hb. As selection of MASC depends on the depletion of CD45 and Gly A+ cells from BM, and cultured MASC are CD45- and GlyA- at all times examined using both FACS and cDNA array analysis, contamination of MASC with hematopoietic cells is very unlikely. We have showed using PCR that the identical retroviral integration specific sequences was present in MASC differentiated to GlyA+ erythroblasts, endodermal, neuroectodermal endothelial and skeletal muscle cells, proving that a single MASC, which is of non-hematopoietic origin, differentiates into primitive erythroblasts, other mesodermal as well as neuroectodermal and endodermal cell types. When undifferentiated human MASC were transplanted into NOD/SCID mice, 0.5-5% of human GlyA+/HLA-class I+ were detected in BM and blood. In conclusion, we demonstrate here for the first time the ex vivo and in vivo differentiation of non-hematopoietic multipotent stem cells from adult human BM into primitive erythrocytes as well as other mesodermal, neuroectodermal and endodermal cell types.

L8 ANSWER 27 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2002:220587 BIOSIS

DN PREV200200220587

TI Characterization of multipotent adult progenitor cells in murine marrow.

AU Jiang, Yuehua [Reprint author]; Reyes, Moryama [Reprint author]; Schwartz,

Robert [Reprint author]; Lenvik, Todd [Reprint author]; Lund, Troy [Reprint author]; Lisberg, Aaron [Reprint author]; Verfaillie, Catherine M. [Reprint author]

CS Medicine, Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 710a. print.

Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 3 Apr 2002  
Last Updated on STN: 3 Apr 2002

AB Until recent, it was thought that tissue specific stem cells could only differentiate into cells of the tissue of origin. However, a number of recent publications have suggested that adult organ specific stem cells may be capable of differentiating into cells of different tissues. We have recently shown that a rare cell within mesenchymal stem cell (MSC) cultures from human marrow can be culture expanded for >80 population doublings. This cell, termed multipotent adult progenitor cell or MAPC, differentiates not only into mesenchymal cells but also endothelium and neuroectoderm. We here describe MAPC from mouse marrow. We initially used methods identical to those used for human cells (culture with EGF and PDGF-BB) to isolate and culture expand MASCs from murine marrow, but MAPC could not be isolated. However, when mouse CD45-/GlyA- cells were cultured in the presence of not only EGF and PDGF-BB, but also LIF, known to be required for murine but not human ES cell culture, cultures of CD13+, CD34-, CD44-, class-I and class-II MHC-, Flk1low MAPC could be established. MAPC have been maintained for >120 population doublings, without telomere shortening.

Real-time PCR showed presence of Oct4 and Rex1 mRNA, two transcription

factors important in maintaining an undifferentiated status of ES cells.

VEGF induced differentiation of mouse MAPC into endothelium (vWF, Tie, Tek, CD31, CD62E positive) that form vascular tubes in vitro.

In addition differentiation to NF200, MAP2, Tau and NSE positive neurons,

GFAP positive astrocytes and MBP positive oligodendrocytes could be

induced using bFGF. Finally, FGF4 and HGF induced differentiation to

albumin, cytokeratin-18, HNF1 and HNF4 positive hepatocytes, that produce

urea in vitro (abstract Schwartz et al). We have established 'clonal'

cell lines, as shown by retroviral marking studies, and found that

differentiation to mesoderm, ectoderm and endoderm occurs from a single

MAPC. Thus, we identified a subpopulation of MSC that can be expanded without senescence and differentiates, at the single cell level,

in vitro to mesoderm, neuroectoderm and endoderm. As discussed in other

abstracts, MAPC engraft and differentiate to hematopoietic cells and epithelial cells in non-injured mice, and contribute to all tissues

when injected in a blastocyst. MAPC therefore hold great promise for the treatment of congenital or degenerative diseases.

L8 ANSWER 28 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on  
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AN 2002:198992 BIOSIS

DN PREV200200198992

TI Engraftment and tissue specific differentiation of multipotent adult

progenitor cells from human marrow in epithelium, the hematopoietic system

and endothelium in vivo.

AU Reyes, Morayma [Reprint author]; Jahagirdar, Balkrishna; Koodie, Lisa;

Verfaillie, Catherine M.

CS Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 547a. print.

Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,

Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)

LA English

ED Entered STN: 20 Mar 2002  
Last Updated on STN: 20 Mar 2002

AB We have identified a rare marrow derived stem cell, termed multipotent adult progenitor cell or MAPC, that co-purifies with mesenchymal stem cells (MSC). Compared with MSC, MAPC can be expanded significantly more (>100 population doublings) without obvious senescence ex vivo. In vitro, MAPC can at the single cell level differentiate to skeletal myoblasts, endothelial cells, neuroectodermal cells and endodermal cells. In contrast, MSC differentiate only in mesenchymal cell types. A number of studies have reported that MSC engraft in mesenchymal tissues, and may engraft in the brain when injected in the brain parenchyma. As human MAPC have greater differentiation potential in vitro, we here tested whether they would engraft in a broader range of tissues in vivo. 106 human MAPC were injected as a bolus intravenously into non-irradiated NOD/SCID mice. 12 weeks after transplant, mice were sacrificed and multiple organs analyzed by immunofluorescence analysis for human specific antigens (anti-human b2-microglobulin or anti-human nuclei antibodies), and using tissue specific antibodies to demonstrate in vivo differentiation in response to organ specific cues. We found 18-25% engraftment of hMAPC in the crypts and villi of the small intestine. Human cells costained with an pan-cytokeratin (CK) antibody. In the lung, hMAPC were seen in 27% of alveoli and 10% of bronchi. Again, human cells co-stained with a pan-CK antibody. In the liver, human cells could be seen scattered through the liver parenchyma and some human binucleated cells were seen that coexpressed pan-cytokeratin at the cellular boundaries. Also in the liver, MAPC were seen clustered in biliary ducts that double labeled with a pancytokeratin antibody. Finally, 5% b2-microglobulin/HLA-class-I positive cells were seen in the bone marrow.

50% of the HLA-class-I+ cells also stained positive with a human specific anti-Glycophorin-A (GlyA) antibody (indicating erythroid differentiation), and 30% of the HLA-class-I positive/GlyA negative cells stained positive for vWF (indicating endothelial differentiation). Up to 10% of cells in the peripheral blood stained positive for human HLA-class-I and human GlyA. Finally, human endothelial cells were seen in the vasculature of a murine, host, thymic lymphoma. Studies are ongoing to determine if engraftment took place in muscle, heart and brain. In addition, marrow from primary engrafted animals is being serially transferred to secondary recipients to determine self renewal occurs of the human cells in vivo. In conclusion, we report here the engraftment and in vivo differentiation of human MAPC into epithelial cells of the lung, liver and small intestine as well as blood and endothelium.

L8 ANSWER 29 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2002:198989 BIOSIS  
DN PREV200200198989

TI Multipotent cells derived from adult mouse marrow engraft in a non-injured recipient and differentiate into hematopoietic, epithelial and endothelial tissues.

AU Jahagirdar, Balkrishna N. [Reprint author]; Jiang, Yuehua [Reprint author]; Reyes, Morayma [Reprint author]; Balckstad, Mark [Reprint author]; Du, Jingbo [Reprint author]; Aldrich, Sara [Reprint author]; Verfaillie, Catherine M. [Reprint author]

CS Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 547a. print.

Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.  
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)

LA English

ED Entered STN: 20 Mar 2002  
Last Updated on STN: 20 Mar 2002

AB We have identified multipotent cells in post-natal human and murine bone marrow, termed multipotent adult progenitor cells (MAPC), that differentiate into cells of ectodermal, mesodermal and endodermal origin in vitro in response to tissue specific cytokines (abstracts Jiang et al).

Here we describe the in vivo behavior of undifferentiated mouse MAPC. 106 MAPC, from beta-galactosidase (b-gal) transgenic ROSA26 mice, were infused via tail vein injection into 4-6 week-old NOD-SCID mice (N=14) with or without sub-lethal irradiation (250 cGy). Animals were sacrificed at 4 to 24 weeks after MAPC injection. Blood, marrow, spleen, liver, intestine, kidney, lung, cardiac and skeletal muscle and brain of the recipients were analyzed for engraftment of b-gal/Neomycin resistance (NEO) transgene containing cells by quantitative PCR for NEO and by immunohistochemistry using a FITC conjugated anti-b-gal antibody. Tissues were co-stained for tissue specific antigens to confirm in vivo differentiation of the donor MAPC. 1-12% engraftment was seen in marrow, spleen, blood and epithelial tissues of all recipients. No engraftment was seen in skeletal muscle, myocardium or brain. In all recipients b-gal+ donor cells expressed markers typical for the tissue in which they had incorporated.

b-gal+ cells in the blood, marrow and spleen co-stained for CD45, TER119, CD19, Gr1 and Mac1 antigens. In the spleen donor cells were found in clusters and not as single cells. In the liver, donor cells formed cords of pan-cytokeratin (CK)+ and albumin+ hepatocytes. In the intestine, b-gal+/pan-CK+ donor cells covered the epithelial surfaces of the two villi arising from a single crypt. In the lung alveoli and bronchi with several b-gal+/pan-CK+ donor cells were found. Irradiation enhanced MAPC engraftment and differentiation into the hematopoietic

lineage and epithelium of intestine and lung, but had no effect on the degree of engraftment in the liver. Engraftment levels were relatively constant when recipients were analyzed after 4 to 24 weeks. 107 unfractionated marrow cells from two animals with 6-8% engraftment were serially transplanted into 2 secondary recipients following 250 cGy radiation. Chimerism in the secondary recipients was similar to that in the primary hosts. No tumors were seen, except in one animal that developed lymphoma of recipient B-lymphocyte origin. Endothelial cells in the tumor were in part of donor origin. In conclusion, MAPC engraft in non-irradiated and irradiated mice and differentiate in vivo into hematopoietic cells, epithelium of liver, lung and intestine and endothelium. Organs with low cell turnover in the absence of damage, such as skeletal and cardiac muscles, brain, and kidney, did not have donor MAPC engraftment. MAPC may therefore be good source of cells for tissue repair.

L8 ANSWER 30 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2002:241253 BIOSIS

DN PREV200200241253

TI The in utero transfer of murine multipotent adult progenitor cells (MAPCs)

result in brain and liver differentiation.

AU Tolar, Jakub [Reprint author]; Jiang, Yuehua [Reprint author]; McElmurry,

Ron [Reprint author]; Jahagirdar, Balkrishna [Reprint author]; Blackstad,

Mark [Reprint author]; Verfaillie, Catherine M. [Reprint author]; Blazar,

Bruce R. [Reprint author]

CS Departments of Pediatrics and Medicine, University of Minnesota and Stem

Cell Institute, Minneapolis, MN, USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 475a. print.

Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,

Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 17 Apr 2002

Last Updated on STN: 17 Apr 2002

AB Recently, we have identified murine MAPCs capable of differentiating in

vitro into multiple cell types including cartilage, bone, fat, muscle and

endothelium (mesoderm), neuroectoderm and endoderm. We hypothesize that

the fetus would represent an ideal setting for in vivo differentiation of

MAPCs, consistent with a high proliferative rate of cells within the fetus

and widespread cellular migratory patterns which may permit access of

MAPCs to sites such as the brain that are not readily accessible post-natally. BALB/c-SCID fetuses were injected at E15/16 with murine

MAPCs (3X10<sup>5</sup> cells) from C57BL/6J-rosa26 (Rosa 26) mice transgenic for

lacZ and neomycin resistance (NeoR) genes. Mice were sacrificed 1d (N=3),

8 wks (N=2) and 14 wks (N=3) postnatally. Cryosections were incubated

with FITC-conjugated anti beta-galactosidase antibody (LacZ-FITC).

Quantitative PCR (qPCR) for NeoR gene expression was performed on sagittal

sections of whole mouse mountings obtained from 1d or 8 wk old recipients.

qPCR analysis revealed that 1.7% and 12.4% of the total DNA from 8 wk old

vs <0.1% of 1d old mice was of Rosa 26 origin, based upon normalization to

control murine MAPCs cells. For 14 wk old mice, tissue sections were

stained for immunofluorescence and adjacent sections were analyzed by

qPCR. Brain engraftment ranged from 0.2 to 1.3% normalized to Rosa 26

MAPC cells, in contrast to the absence of brain engraftment after post-natal MAPC infusion. Using dual color immunofluorescence

staining we were able to show co-localization of beta-galactosidase and

glial fibrillary acidic protein. Albumin co-staining liver cells derived

from Rosa 26 MAPCs were present, albeit infrequently. Analyses are

ongoing and will be presented quantifying the potential differentiating



capacity of MAPCs into multiple tissues of mesodermal, ectodermal, and endodermal origin. In summary, we show for the first time that murine MAPCs engraft and differentiate into brain and liver cells after in utero transfer. Our results support the possibility of future clinical use of MAPCs in attempts to correct neurological, hepatic, and possibly other types of congenital disorders pre-natally.

L8 ANSWER 31 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2001:486589 BIOSIS

DN PREV200100486589

TI Identification and transplantation of a novel, multipotent neural stem

cell from mammalian skin.

AU Toma, J. G. [Reprint author]; Akhavan, M. [Reprint author]; Fernandes, K.

[Reprint author]; Fortier, M. [Reprint author]; Wang-Ninio, Y. [Reprint

author]; Barnabe-Heider, F. [Reprint author]; Sadikot, A.; Kaplan, D. R.;

Miller, F. D. [Reprint author]

CS Centre for Neuronal Survival, Montreal Neurological Institute, McGill

University, Montreal, PQ, Canada

SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 57. print.

Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San

Diego, California, USA. November 10-15, 2001.

ISSN: 0190-5295.

DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 17 Oct 2001

Last Updated on STN: 23 Feb 2002

AB Here we describe the isolation of neural stem cells from juvenile and

adult rodent skin. These cells, which are called SKPs (SKin-derived

Precursors) derive from the dermis, express nestin and fibronectin, and

can be passaged for over one year without altering their phenotype. When

differentiated in culture, SKPs can generate cells of both neural and

mesodermal origin; neurons, glial cells, smooth muscle cells and

adipocytes. Moreover, clones of single cells can be expanded, and will still generate all of these different progeny. When transplanted into the neonatal or adult brain, SKPs survive, migrate, and differentiate into morphologically complex cells. Finally, similar precursors that express neuron-specific proteins upon differentiation can be isolated from adult human scalp. Since these cells are distinct from both CNS-derived neural stem cells and from mesenchymal stem cells, but can generate both neural and mesodermal progeny, we propose that they represent a novel multipotent adult stem cell and suggest that skin may provide an accessible, autologous source of stem cells for transplantation.

L8 ANSWER 32 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2000:505369 BIOSIS

DN PREV200000505369

TI Reliability of an air-braked ergometer to record peak power during a maximal cycling test.

AU Balmer, James [Reprint author]; Davison, R. C. Richard; Bird, Steve R.

CS Department of Sport Science, Canterbury Christ Church University College, Canterbury, CT1 1QU, UK

SO Medicine and Science in Sports and Exercise, (October, 2000) Vol. 32, No. 10, pp. 1790-1793. print. CODEN: MSPEDA. ISSN: 0195-9131.

DT Article

LA English

ED Entered STN: 22 Nov 2000

Last Updated on STN: 11 Jan 2002

AB Purpose: To assess the reliability of the Kingcycle™ ergometer, this

study compared peak power recorded using a Kingcycle and SRMTM power

meters during Kingcycle maximal aerobic power tests. Methods: The study

was completed in two parts: for part 1, nine subjects completed three

maximal tests with a stabilizing kit attached to the Kingcycle rig and

calibration of the Kingcycle checked against SRM (MAPC); and for part 2, nine subjects completed two maximal tests without the stabilizing

kit and the Kingcycle calibrated using the standard procedure (MAPS).

Each MAPC test was separated by 1 wk; however, MAPS tests were separated by 54  $\pm$  32 d, (mean  $\pm$  SD). Testing procedure was repeated for

each MAP and peak power output was calculated as the highest average power

output recorded during any 60-s period of the MAP test using the Kingcycle

(KingPPO) and SRM (SRMPPO). Results: Coefficient of variations (CVs) for

KingPPO were larger than those of SRMPPO; 2.0% (95%CI = 1.5-3.0) versus

1.3% (95%CI = 1.0-2.0) and 4.6% (95%CI = 2.7-7.6) versus 3.6% (95%CI =

2.1-6.0) for MAPC and MAPS, respectively. During all tests,

KingPPO was higher than SRMPPO by an average of approx 10% ( $P < 0.001$ ).

Conclusions: Investigators should be aware of the discrepancy between the

two systems when assessing peak power and that SRM cranks provide a more

reproducible measure of peak power than the Kingcycle ergometer.

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DUPLICATE 4

AN 2000:32719 BIOSIS

DN PREV200000032719

TI Tumor burden and clonality in multiple intestinal neoplasia mouse/normal

mouse aggregation chimeras.

AU Novelli, Marco R. [Reprint author]; Wasan, Harpreet; Rosewell, Ian; Bee,

Julie; Tomlinson, Ian P.; Wright, Nicholas A.; Bodmer, Walter F.

CS Department of Histopathology, University College London, London, WC1E 6JJ,

UK

SO Proceedings of the National Academy of Sciences of the United States of

America, (Oct. 26, 1999) Vol. 96, No. 22, pp. 12553-12558. print.

CODEN: PNASA6. ISSN: 0027-8424.

DT Article

LA English

ED Entered STN: 13 Jan 2000

Last Updated on STN: 31 Dec 2001

AB Aggregation chimeras were formed between C57BL/6 mice heterozygous for the

Apcmin (Min) mutation and wild-type SWR mice, that differ in their Pla2g2a

status, a modifier of Apcmin, and also in their resistance to intestinal

polyp formation. Variation in the dolichos biflorus  
 agglutinin-staining  
 patterns of the intestines of these mouse strains was used to  
 determine  
 the chimeric composition of the intestine in individual mice and  
 to  
 examine the clonal composition of adenomas. Macroscopic adenoma  
 numbers  
 in chimeric mice were compared with the expected adenoma numbers  
 based on  
 the percentage of C57BL/6J-Apcmin/+ epithelium in individual  
 mice. These  
 results unexpectedly show that there was no apparent inhibitory  
 effect of  
 the SWR-derived (Pla2g2a wild-type) tissue on adenoma formation  
 in the  
 C57BL/6J-Apcmin/+ epithelium. This suggests that the main  
 genetic  
 modifiers of the Min phenotype act at a cellular or  
 crypt-restricted level  
 with no discernable systemic effect. All adenomas were seen to  
 contain  
 C57BL/6J-Apcmin/+ -derived epithelium, confirming that the  
 germ-line  
 mutation of the mApc gene is necessary to initiate tumorigenesis  
 in this model system, and that the mApc gene acts in a cell  
 autonomous fashion.

L8 ANSWER 34 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson  
 Corporation on  
 STN DUPLICATE 5  
 AN 2000:14771 BIOSIS  
 DN PREV200000014771  
 TI The effect of the chemical structure of the phospholipid polymer  
 on  
 fibronectin adsorption and fibroblast adhesion on the gradient  
 phospholipid surface.  
 AU Iwasaki, Yasuhiko [Reprint author]; Sawada, Shin-ichi;  
 Nakabayashi, Nobuo;  
 Khang, Gilson; Lee, Hai Bang; Ishihara, Kazuhiko  
 CS Institute of Biomaterials and Bioengineering, Tokyo Medical and  
 Dental  
 University, 2-3-10 Kanda-surugadai, Chiyoda-ku, Tokyo, 101-0062,  
 Japan  
 SO Biomaterials, (Nov., 1999) Vol. 20, No. 22, pp. 2185-2191.  
 print.  
 CODEN: BIMADU. ISSN: 0142-9612.  
 DT Article  
 LA English  
 ED Entered STN: 29 Dec 1999  
 Last Updated on STN: 31 Dec 2001  
 AB The interaction between biocomponents and the polyethylene (PE)  
 surface

modified with poly(omega-methacryloyloxyalkyl phosphorylcholine (MAPC)) was considered taking into account the surface characteristics, i.e., density, mobility, and orientation of the poly(MAPC). The PE surface, grafted gradually with the poly(MAPC) was prepared by corona irradiation method. The amount of peroxide produced on the PE surface which was determined with 1,1-diphenyl-2-picryl-hydrazyl, increased with an increase in the energy of the corona. The surface density of the poly(MAPC) was increased with an increase in the amount of the peroxides produced by the corona irradiation. The orientation and mobility of the poly(MAPC) grafted on the PE surface was evaluated with 1,6-diphenyl-1,3,5-hexatriene. The orientation of the poly(6-methacryloyloxyhexyl phosphorylcholine (MHPC)) which has six methylene chains between the phospholipid polar group and the backbone was higher than that of other poly(MAPC)s. The mobility of the poly(MAPC) decreased with an increase in the methylene chain length in the MAPC unit. The fibronectin adsorption on the gradient PE sheet grafted with poly(MAPC) was determined with enzyme-labeled immunoassay. The amount of adsorbed fibronectin on the PE grafted with poly(2-methacryloyloxyethyl phosphorylcholine(MPC)) and poly(MHPC) decreased with an increase in their surface density. Especially, the PE sheet grafted with the poly(MHPC) was effectively reduced compared with other poly(MAPC)s. On the poly(10-methacryloyloxydecyl phosphorylcholine (MDPC)), there is a minimum amount of adsorbed fibronectin. The fibronectin adsorption pattern on the PE sheet grafted with poly(MAPC) was quite different from the chemical structure of the MAPC unit. The human normal diploid fibroblasts (WI-38 cells) were cultured on the gradient PE sheet grafted with poly(MAPC) changing the concentration of seeded WI-38 cells. The adhesion behavior of the WI-38 cells was different depending on the concentration of the seeded WI-38 cells. When the concentration was low, the number of the adherent WI-38 cells had the same tendency as fibronectin adsorption. The gradient PE sheet grafted with the poly(MHPC) effectively reduced WI-38 cells adhesion even when the concentration of the WI-38 cells was high. The biocompatibility of polymer surfaces can be

improved by highly oriented phosphorylcholine group.

L8 ANSWER 35 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN  
AN 1999:392330 CAPLUS  
DN 131:35798  
TI Surface modified poly(methyl methacrylate) with  
1-methyl-2-methacrylamidoethyl phosphorylcholine moiety  
AU Sugiyama, Kazuo; Ohga, Koji  
CS Dep. Industrial Chemistry, Faculty Engineering, Kinki Univ.,  
Higashi-Hiroshima, 739, Japan  
SO Macromolecular Chemistry and Physics (1999), 200(6), 1439-1445  
CODEN: MCHPES; ISSN: 1022-1352  
PB Wiley-VCH Verlag GmbH  
DT Journal  
LA English  
AB A series of poly(Me methacrylate) [poly(MMA)] microspheres  
covered with  
the 1-methyl-2-methacrylamidoethyl phosphorylcholine (MAPC)  
moiety, poly(MAPC-co-MMA), were prepared by emulsifier-free  
emulsion copolymn. of Me methacrylate (MMA) and MAPC using  
potassium peroxy-disulfate (KPS) or  
2,2'-azobis[2-(imidazolin-2-yl)propane] dihydrochloride (ABIP) as  
initiators. The  $\zeta$ -potentials of the particles are -72 to -26  
mV and  
0 to 27 mV for poly(MAPC-co-MMA) produced by KPS and ABIP, resp.  
Poly(MAPC-co-MMA) suppresses the adsorption of albumin,  
 $\gamma$ -globulin, and fibrinogen more than poly(MMA) as the control.  
From  
XPS measurements the MAPC moiety and the fragments of the  
initiator are located on the surface of the polymer films  
prepared from  
poly(MAPC-co-MMA). Egg yolk lecithin adsorbs on the surface of  
the films, and an organized adsorption layer of lipid, i.e., a  
hydrogel  
layer with an analogous structure to biomembrane, is formed.  
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 36 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson  
Corporation on  
STN  
AN 1999:300283 BIOSIS  
DN PREV199900300283  
TI Competitive adsorption between phospholipid and plasma protein  
on a  
phospholipid polymer surface.  
AU Iwasaki, Yasuhiko [Reprint author]; Nakabayashi, Nobuo;  
Nakatani, Masako;  
Mihara, Takashi; Kurita, Kimio; Ishihara, Kazuhiko  
CS Institute for Medical and Dental Engineering, Tokyo Medical and  
Dental  
University, 2-3-10, Kanda-surugadai, Chiyoda-ku, Tokyo,  
101-0062, Japan

DUPLICATE 6

SO Journal of Biomaterials Science Polymer Edition, (1999) Vol. 10,  
 No. 5, pp. 513-529. print.  
 CODEN: JBSEEA. ISSN: 0920-5063.

DT Article

LA English

ED Entered STN: 12 Aug 1999  
 Last Updated on STN: 12 Aug 1999

AB The competitive adsorption of proteins and phospholipids on  
 omega-methacryloyloxyalkyl phosphorylcholine (MAPC) polymer was  
 evaluated in this study. Albumin, fibrinogen, and dimyristoyl  
 phosphatidylcholine (DMPC) were used as model components. The  
 amount of  
 DMPC adsorbed on the MAPC polymers increased with an increase in  
 the MAPC unit composition of the polymer. The methylene chain  
 length of the MAPC unit was another factor influencing the DMPC  
 adsorption when the MAPC unit composition of the MAPC  
 polymer was low. The state of albumin and DMPC liposome  
 adsorbed on the  
 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer was  
 determined by  
 dynamic contact angle (DCA) measurement. The adsorption  
 strength of  
 albumin on the MPC polymer was weaker than that on the  
 poly(n-butyl  
 methacrylate (BMA)), that is, the albumin was detached from the  
 MPC  
 polymer during the rinsing process. On the poly(BMA) surface, no  
 difference in the shape of the DCA loops before and after  
 contact with the  
 DMPC liposomal suspension was observed. Fibrinogen adsorption  
 on the  
 MAPC polymer was detected by gold-colloid labeled immunoassay.  
 The amount of fibrinogen adsorbed on every MAPC polymer surface  
 was reduced by addition of the DMPC liposome in the fibrinogen  
 solution.  
 The number of platelets adhered on the MAPC polymer was also  
 decreased when the DMPC liposome was present in the fibrinogen  
 solution  
 during pretreatment. We concluded that phospholipids were  
 preferentially  
 adsorbed on the MAPC polymer surface compared with plasma  
 protein and that the adsorbed phospholipids played an important  
 role in  
 showing an excellent blood compatibility on the MAPC polymer.

L8 ANSWER 37 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson  
 Corporation on  
 STN  
 AN 1999:342613 BIOSIS  
 DN PREV199900342613  
 TI Behavior of blood cells in contact with water-soluble  
 phospholipid

DUPLICATE 7

polymer.

AU Iwasaki, Yasuhiko [Reprint author]; Ijuin, Mika; Mikami, Asako; Nakabayashi, Nobuo; Ishihara, Kazuhiko

CS Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental

University, 2-3-10, Kanda-Surugadai, Chiyoda-ku, Tokyo, 101-0062, Japan

SO Journal of Biomedical Materials Research, (Sept. 5, 1999) Vol. 46, No. 3, pp. 360-367. print.  
CODEN: JBMRBG. ISSN: 0021-9304.

DT Article

LA English

ED Entered STN: 24 Aug 1999

Last Updated on STN: 24 Aug 1999

AB omega-Methacryloyloxyalkyl phosphorylcholine (MAPC) polymer, which has various methylene chain lengths between the phosphorylcholine

group and the backbone, was synthesized with attention to formation of the

biomembrane. The effect of water-soluble poly(MAPC) on the function and activation of blood cells was evaluated to determine the

interaction between blood cells and the MAPC polymer. The poly(MAPC) and the MAPC copolymer with a small amount of fluorescent units were synthesized by a conventional radical polymerization technique. Using a fluorescence spectrometer, it was

determined that the MAPC polymer was adsorbed on the plasma membrane of platelets when the platelets were suspended in an aqueous

solution of the MAPC copolymer. The hemolytic activity of poly(MAPC) was less than that of other water-soluble polymers, such as poly(ethylene glycol) and poly(1-vinyl-2-pyrrolidone) (PVPy). The change

in the plasma membrane fluidity of platelets on contact with poly(MAPC) was determined with 1,6-diphenyl-1,3,5,-hexatriene. The

plasma membrane fluidity of platelets decreased with an increase in the

methylene chain length of the MAPC unit. The aggregation activity of platelets after contact with poly(MAPC) was also evaluated, but no significant difference between that of polymer-contacted

platelets and native platelets was observed. Finally, the activity of

platelets on contact with poly(MAPC) was determined by measuring the cytoplasmic calcium ion concentration ((Ca<sup>2+</sup>)<sub>i</sub>) in platelets. The

increase in (Ca<sup>2+</sup>)<sub>i</sub> in the platelets after contact with poly(MAPC) was similar to that of native platelets. We conclude that the poly(MAPC) reduced platelet activation even though the poly(MAPC)

reduced platelet activation even though the poly(MAPC)



MAPC) adsorbed on the membrane surface of the platelets. In particular, poly(10-methacryloyloxydecyl phosphorylcholine) significantly reduced platelet activation compared with PVPy.

L8 ANSWER 38 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2000:42367 CAPLUS

DN 132:66084

TI A state space model based multistep adaptive predictive controller (

MAPC) with disturbance modeling and Kalman filter prediction

AU Sripada, N. Rao; Fisher, D. Grant

CS Department of Chemical Engineering, Indian Institute of Technology,  
Madras, 600 036, India

SO Indian Journal of Chemical Technology (1999), 6(4), 225-236  
CODEN: ICHTEU; ISSN: 0971-457X

PB National Institute of Science Communication, CSIR

DT Journal

LA English

AB A multistep adaptive predictive control strategy based on a state space

model of the process has been developed. It can be compared with the

generalized predictive control algorithm. The emphasis in the development

of the proposed control scheme is on modeling and elimination of disturbances. In the proposed scheme any prior information regarding the

disturbances can be incorporated (by specifying certain polynomials and/or

the noise covariances). If no prior information is available then the

unknown un-modeled effects (such as noise, unmeasured load-disturbances

and model process mismatch) can be represented by a residual model which

can best be identified in a two-stage setting. This approach leads to

satisfactory modeling of disturbances and good regulation via predictive

control. Some important features of the proposed algorithm are:

(i) it

uses a state space model which allows sep. modeling of u-to-y process

dynamics, process and measurement noise; this is not possible in an

ARMAX-type input/output model where process and measurement noise appear

lumped in the noise polynomial; (ii) it uses a Kalman Filter (KF) to

generate the predictions of the output; the KF can be easily tuned via

noise covariances and is a simpler and better alternative to specifying or estimating a noise polynomial; (iii) there is no need to solve a Diophantine identity online; the result is reduced computation; and (iv) if residual modeling is used it leads to simpler and improved way of handling disturbances. The proposed control algorithm is presented for the single-input, single-output case. Applying the algorithm to multivariable processes is straightforward. Simulation examples are included to illustrate the advantages and performance of the proposed control scheme.

RE.CNT 24        THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
                 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8    ANSWER 39 OF 88    BIOSIS    COPYRIGHT (c) 2009 The Thomson  
Corporation    on  
              STN

AN    1999:308399    BIOSIS

DN    PREV199900308399

TI    Polyp number and clonality in multiple intestinal neoplasia mouse  
aggregation chimaeras.

AU    Novelli, M. R. [Reprint author]; Wasan, H.; Rosewell, I.; Bee,  
J.;

              Tomlinson, I. A.; Wright, N. A.; Bodmer, W. F.

CS    Department of Histopathology, University College London, London,  
UK

SO    Journal of Pathology, (1999) Vol. 187, No. SUPPL., pp. 34A.  
print.

              Meeting Info.: 178th Meeting of the Pathological Society of  
Great Britain

              and Ireland. Cambridge, England, UK. January 6-8, 1999.

Pathological

              Society of Great Britain and Ireland.

              CODEN: JPTLAS. ISSN: 0022-3417.

DT    Conference; (Meeting)

              Conference; Abstract; (Meeting Abstract)

LA    English

ED    Entered STN: 12 Aug 1999

              Last Updated on STN: 12 Aug 1999

L8    ANSWER 40 OF 88    BIOSIS    COPYRIGHT (c) 2009 The Thomson  
Corporation    on

              STN

DUPLICATE 8

AN    1998:429072    BIOSIS

DN    PREV199800429072

TI    Platelet adhesion on the gradient surfaces grafted with  
phospholipid  
              polymer.

AU Iwasaki, Yasuhiko [Reprint author]; Ishihara, Kazuhiko;  
 Nakabayashi,  
 Nobuo; Khang, Gilson; Jeon, Ju Hyeong; Lee, Jin Whan; Lee, Hai  
 Bang

CS Inst. Med. Dent. Eng., Tokyo Med. Dent. Univ., 2-3-10  
 Kanda-Surugadai,  
 Chiyoda-ku, Tokyo 101-0062, Japan

SO Journal of Biomaterials Science Polymer Edition, (1998) Vol. 9,  
 No. 8, pp. 801-816. print.  
 CODEN: JBSEEA. ISSN: 0920-5063.

DT Article

LA English

ED Entered STN: 7 Oct 1998  
 Last Updated on STN: 7 Oct 1998

AB We have synthesized omega-methacryloyloxyalkyl phosphorylcholine  
 (  
 MAPC) polymers as new blood-compatible materials, with attention  
 to the surface structure of the biomembrane and investigated  
 their blood  
 compatibility. The blood compatibility observed on the MAPC  
 polymers is due to their strong affinity to phospholipids. When  
 the blood  
 comes in contact with the MAPC polymer, phospholipids in the  
 plasma preferentially adsorb on the surface, compared with the  
 plasma  
 proteins or cells. The adsorbed phospholipids construct a  
 biomembrane-like structure on the MAPC polymer surface. The  
 MAPC polymers then have an excellent blood compatibility. In  
 this  
 study, we prepared a gradient poly(MAPC)-grafted polyethylene  
 (PE) surface using a corona discharge treatment method to  
 clarify the  
 effect of the chemical structure of the MAPC unit on the blood  
 compatibility of the MAPC polymers. The surface composition of  
 MAPC and the hydrophilicity on the poly(MAPC)-grafted PE  
 surface were determined by X-ray photoelectron spectroscopic  
 (XPS)  
 analysis and contact angle measurement with water, respectively.  
 The  
 phosphorus/carbon (P/C) ratio determined by the XPS analysis  
 increased,  
 but the water contact angle decreased with increasing corona  
 irradiation  
 energy. These results indicated that the surface density of the  
 MAPC unit was increased. More than 2.5 cm from the starting  
 point  
 of the corona irradiation, the P/C ratio and water contact angle  
 of the  
 surface achieved a constant level. Thus, the surface was  
 completely  
 covered with the grafted poly(MAPC) chain. The effect of the  
 methylene chain length of the MAPC unit on surface properties

was also observed. The phospholipid polar group of the MAPC unit was effectively exposed on the surface as the chain length became longer. Moreover, the hydrophobicity of the surface was increased with the increase in the methylene chain length of the MAPC unit. The number of platelets adhering to the poly(MAPC)-grafted PE surface was reduced from the same point where the P/C ratio became constant.

L8 ANSWER 41 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on

STN

DUPLICATE 9

AN 1998:485747 BIOSIS

DN PREV199800485747

TI Desethylamiodarone prolongation of cardiac repolarization is dependent on

gene expression: A novel antiarrhythmic mechanism.

AU Drvota, Viktor [Reprint author]; Blange, Irina; Haggblad, Johan; Sylven,

Christer

CS Dep. Cardiol., M52, Huddinge Univ. Hosp., S-141 86 Huddinge, Sweden

SO Journal of Cardiovascular Pharmacology, (Oct., 1998) Vol. 32, No. 4, pp. 654-661. print.

CODEN: JCPCDT. ISSN: 0160-2446.

DT Article

LA English

ED Entered STN: 5 Nov 1998

Last Updated on STN: 5 Nov 1998

AB Desethylamiodarone (DEA) is the major metabolite of amiodarone and has

similar electrophysiologic effects with prolongation of the repolarization

that is reversed by thyroid hormone (T3). Some of the electrophysiologic

effects are probably due to antagonism of T3 at the receptor level. Such

effects of T3 are mediated by modulation of gene transcription. The aim

of this study was to investigate whether cycloheximide (Cy), an inhibitor

of protein synthesis, and actinomycin D (ActD), a RNA-synthesis inhibitor,

block DEA-induced prolongation of the repolarization and whether DEA takes

part in the autoregulation of the nuclear thyroid hormone-receptor

subtypes (ThR). Corrected monophasic action potentials (MAPc) and QTc were measured in Langendorff-perfused guinea pig hearts

for 1 h.

The hearts were continuously perfused with (a) vehicle, (b) 7.5  $\mu$ M Cy, (c) 5  $\mu$ M DEA, (d) 5  $\mu$ M DEA + 7.5 WV Cy, (e) 1  $\mu$ M T3, (f) 5  $\mu$ M DEA + 1  $\mu$ M T3, (g) 1.5  $\mu$ M ActD, and (h) ActD + DEA. A potassium channel blocker with class III antiarrhythmic effects, 0.5  $\mu$ M almokalant, was used as a control, separately and together with Cy. Western blot analysis for the ThR subtypes  $\alpha$ ,  $\beta$ 1, and  $\beta$ 2 was performed on vehicle and DEA-treated hearts. DEA increased MAPc by 19% ( $p < 0.0005$ ) and QTc by 18% ( $p < 0.0005$ ). There was no effect on MAPc or QTc when Cy, ActD, or T3 was added with DEA. Almokalant increased MAPc by 14% ( $p < 0.005$ ) and QTc by 13% ( $p < 0.0005$ ). When Cy was present, almokalant still induced a similar prolongation of MAPc by 14% ( $p < 0.005$ ) and QTc by 17% ( $p < 0.0005$ ). Western blot analysis revealed no change in the expression of the ThR protein. In conclusion, the prolongation of the cardiac repolarization by DEA, but not almokalant, can be totally blocked by Cy and ActD. This indicates that the class III action of DEA is at least in part dependent on transcription rather than a direct effect on cell-membrane channels or receptors. The action of DEA could be reversed by T3, indicating an antagonism between DEA and T3. These results suggest a new antiarrhythmic mechanism dependent on gene expression.

L8 ANSWER 42 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on

STN

DUPLICATE 10

AN 1997:434403 BIOSIS

DN PREV199799733606

TI Reduction of surface-induced platelet activation on phospholipid polymer.

AU Iwasaki, Yasuhiko [Reprint author]; Mikami, Asako; Kurita, Kimio; Yui,

Nobuhiko; Ishihara, Kazuhiko; Nakabayashi, Nobuo

CS Inst. Med. Dental Engineering, Tokyo Med. Dental Univ., 2-3-10 Kanda-surugadai, Chiyoda-ku, Tokyo 101, Japan

SO Journal of Biomedical Materials Research, (1997) Vol. 36, No. 4, pp. 508-515.

CODEN: JBMRBG. ISSN: 0021-9304.

DT Article

LA English

ED Entered STN: 8 Oct 1997

Last Updated on STN: 21 Nov 1997

AB     omega-Methacryloyloxyalkyl phosphorylcholine (MAPC) polymers which have been synthesized with attention to the surface structure of a biomembrane show excellent blood compatibility, i.e., resistance to protein adsorption and blood cell adhesion. To clarify the stability of platelets in contact with the MAPC polymer surfaces, cytoplasmic free calcium concentration ((Ca-2+)-i) in the platelets was measured. A platelet suspension was passed through a column packed with various polymer beads after treatment with plasma, and the (Ca-2+)-i in the platelets eluted from the column was measured. The (Ca-2+)-i in contact with the MAPC polymers, i.e., poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate (BMA)) (PMEB) and poly(6-methacryloyloxyhexyl phosphorylcholine-co-BMA) (PMHB), was less than that in contact with poly(BMA). However, poly(10-methacryloyloxydecyl phosphorylcholine-co-BMA) (PMDB) was not effective in suppressing the increase in (Ca-2+)-i, and thus was at the same level as in the poly(BMA). This result indicated that platelets in contact with PMEB or PMHB were less activated compared with those in contact with PMDB and poly(BMA). Moreover, the state of the platelets adhered to these polymer surfaces, both morphologically and immunologically, was examined. Scanning electron microscopic observation of the polymer surface after contact with a platelet suspension revealed that many platelets adhered and changed their shape on the poly(BMA). The numbers of adherent platelets were reduced on all MAPC polymer surface. The relative amount of alpha-granule membrane glycoprotein (GMP-140) which appears on the cell membrane by activation of platelets on the PMEB surfaces was less than that on poly(BMA) and poly(2-hydroxyethyl methacrylate). These results suggest that PMEB and PMHB suppressed not only platelet adhesion but also activation of the platelets in contact with these surfaces.

L8 ANSWER 43 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 11  
 AN 1997:615547 CAPLUS  
 DN 127:336526  
 OREF 127:65999a,66002a  
 TI Stabilization of liposomes attached to polymer surfaces having  
 phosphorylcholine groups  
 AU Iwasaki, Yasuhiko; Tanaka, Shinobu; Hara, Masahiko; Ishihara,  
 Kazuhiko;  
 Nakabayashi, Nobuo  
 CS Inst. Med. and Dental Eng., Tokyo Med. and Dental Univ., Tokyo,  
 101, Japan  
 SO Journal of Colloid and Interface Science (1997), 192(2), 432-439  
 CODEN: JCISA5; ISSN: 0021-9797  
 PB Academic  
 DT Journal  
 LA English  
 AB The adsorption state of liposomes on a polymer surface  
 containing a  
 phosphorylcholine group, i.e.,  $\omega$ -methacryloyloxyalkyl  
 phosphorylcholine (MAPC) polymer, was evaluated using a quartz  
 crystal microbalance and an atomic force microscope. After a  
 quartz crystal  
 resonator coated with the MAPC polymer or poly[2-hydroxyethyl  
 methacrylate (HEMA)] was equilibrated with distilled water, the  
 quartz  
 crystal was contacted with a dipalmitoylphosphatidylcholine  
 (DPPC)  
 liposomal suspension. The resonance frequency change during  
 liposome  
 adsorption on the poly(HEMA)-coated resonator was larger than  
 that on the  
 MAPC polymer-coated resonator. The temperature response based  
 on the  
 phase transition of adsorbed DPPC liposomes, i.e., the liquid  
 crystalline state  
 to gel state, on the MAPC polymer-coated resonator was more  
 sensitive than that on the poly(HEMA)-coated resonator.  
 Moreover, when the  
 DPPC liposomes adsorbed on the polymer surfaces were  
 disintegrated with a  
 nonionic surfactant, it took longer for the frequency to return  
 to the  
 initial value of the poly-(HEMA)-coated resonator than to that  
 of the  
 MAPC polymer-coated resonator. According to atomic force  
 microscopic  
 observation of the polymer surface after treatment with the  
 liposomal  
 suspension, the DPPC liposomes adsorbed on the MAPC polymers  
 maintained their spherical shape well. We conclude that DPPC  
 liposomes  
 adsorbed on the poly(HEMA) surface can penetrate a hydrated  
 layer and its

ordered structure. On the other hand, DPPC liposomes may adsorb to the

MAPC polymer surface without change in their original structure.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 44 OF 88 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights

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AN 1997141519 EMBASE

TI Two-component signal transducers and MAPK cascades.

AU Wurgler-Murphy, Susannah M. (correspondence); Saito, Haruo

CS Division of Tumor Immunology, Dana-Farber Cancer Institute, Harvard

Medical School, Boston, MA 02115, United States.

haruo\_saito@dfci.harvard.

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AU Wurgler-Murphy, Susannah M. (correspondence)

CS Division Tumor Immunology, Dana-Farber Cancer Institute, Boston, MA 02115,

United States.

SO Trends in Biochemical Sciences, (May 1997) Vol. 22, No. 5, pp. 172-176.

Refs: 38

ISSN: 0968-0004 CODEN: TBSCDB

PUI S 0968-0004(97)01036-0

CY United Kingdom

DT Journal; General Review; (Review)

FS 029 Clinical and Experimental Biochemistry

004 Microbiology: Bacteriology, Mycology, Parasitology and

Virology

LA English

SL English

ED Entered STN: 29 May 1997

Last Updated on STN: 29 May 1997

AB Two-component signal transducers, which are characterized by the histidine-to-aspartate phospho-transfer mechanism, were once thought to be

restricted to prokaryotes. They have, however, now been identified in

diverse eukaryotic species including plant, fungus, yeast and slime mold,

In yeast, a two-component osmosensor has been found to regulate a mitogen-activated protein kinase (MAPK) cascade, a ubiquitous eukaryotic signaling module.

L8 ANSWER 45 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on

STN

DUPLICATE 12

AN 1997:38257 BIOSIS

DN PREV199799330245

TI Effect of reduced protein adsorption on platelet adhesion at the



phospholipid polymer surfaces.

AU Iwasaki, Yasuhiko; Kurita, Kimio; Ishihara, Kazuhiko [Reprint author];

Nakabayashi, Nobuo

CS Inst. Med. Dental Engineering, Tokyo Med. Dental Univ., 2-3-10 Kanda-surugadai, Chiyoda-ku, Tokyo, 101, Japan

SO Journal of Biomaterials Science Polymer Edition, (1996) Vol. 8, No. 2, pp. 151-163.

CODEN: JBSEEA. ISSN: 0920-5063.

DT Article

LA English

ED Entered STN: 28 Jan 1997

Last Updated on STN: 25 Mar 1997

AB We prepared polymers having a phospholipid polar group, poly(omega-methacryloyloxyalkyl phosphorylcholine (MAPC)-co-n-butyl methacrylate(BMA)), as new biomedical materials and evaluated

their blood compatibility with attention to protein adsorption and

platelet adhesion. The total amount of proteins adsorbed on the polymer

surface from human plasma was determined, and the distribution of adsorbed

proteins on the plasma-contacting surface was analyzed. The amount of

proteins adsorbed on every poly(MAPC-co-BMA) was small compared with that observed on polymers without the phospholipid polar group.

However, there was no significant difference in the amount of adsorbed

proteins on the poly(MAPC-co-BMA) even when the methylene chain length between the phospholipid polar group and the backbone in the

MAPC moiety was altered. Platelet adhesion on the polymer surface

from a platelet suspension in a buffered solution was evaluated with and

without plasma treatment on the surface. When a rabbit platelet suspension was brought into contact with the poly(BMA) surface after

treatment with plasma, many platelets adhered and aggregated. However, a

reduced amount of platelet adhered on the poly(BMA) was found in the case

of direct contact with the platelet suspension. On the other hand, the

poly(MAPC-co-BMA)s could inhibit platelet adhesion under both conditions. Based on these results, it can be concluded that the proteins

adsorbed on the surface play an important role in determining the platelet

adhesion and suppression of the protein adsorption on the surface, which

is one of the most significant ways of inhibiting platelet adhesion.

L8 ANSWER 46 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1997:200473 CAPLUS

DN 126:248973

OREF 126:48087a,48090a

TI O<sub>2</sub>-dependent electron flow in intact spinach chloroplasts: properties and

possible regulation of the Mehler-ascorbate peroxidase cycle

AU Schreiber, Ulrich; Hormann, Henning; Asada, Kozi; Neubauer, Christian

CS Lehrstuhl Botanik I, Universitat Wurzburg, Wurzburg, D-97082, Germany

SO Photosynthesis: From Light to Biosphere, Proceedings of the International

Photosynthesis Congress, 10th, Montpellier, Fr., Aug. 20-25, 1995 (

1995), Volume 2, 813-818. Editor(s): Mathis, Paul. Publisher: Kluwer, Dordrecht, Neth.

CODEN: 64DFAW

DT Conference

LA English

AB A brief overview on the properties of the Mehler-ascorbate peroxidase

cycle (MAPC) proves it to be particularly effective in the formation of a regulatory  $\Delta pH$  in intact spinach chloroplasts.

The

effects of low concns. of the uncoupler nigericin on

O<sub>2</sub>-dependent electron

flow and on  $\Delta pH$  formation indicate that the suppression of electron

flow and of the  $\Delta pH$  associated with MAPC activity occurs at

.apprx.10-fold lower nigericin concn than the stimulation of Me viologen-catalyzed O<sub>2</sub>-reduction The effect of ADP-addition on

O<sub>2</sub>-dependent flow

and on the associated  $\Delta pH$  in class D chloroplasts in the presence of

other acceptors further supports the possibility of MAPC

regulation by the energy-status of the thylakoids. The

requirements of O<sub>2</sub>

and ascorbate for  $\Delta pH$ -formation in intact chloroplasts favor a major

role of O<sub>2</sub> in  $\Delta pH$ -formation by the MAPC. In conclusion,

substantial evidence has been accumulated suggested that

O<sub>2</sub>-dependent

electron flow in the MAPC has the potential of generating a large  $\Delta pH$  in intact spinach chloroplasts.

L8 ANSWER 47 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1995:684452 CAPLUS

DN 123:123027

OREF 123:21697a,21700a

TI Ex vivo blood compatibility of polymers having phospholipid polar group

AU Iwasaki, Yasuhiko; Kurita, Kimio; Tanaka, Shinobu; Ishihara, Kazuhiko;

Nakabayashi, Nobuo

CS College Science and Technology, Nihon University, Tokyo, 101, Japan

SO Seitai Zairyo (1995), 13(2), 62-9

CODEN: SEZAEH; ISSN: 0910-304X

PB Nippon Baiomateriaru Gakkai

DT Journal

LA Japanese

AB We have already reported the effects of hydrophobicity of phospholipid

moiety on hemocompatibility, phospholipid polymers (MAPC copolymer) with various methylene chain length between the phosphorylcholine group and main chain of the copolymer were prepared and

their characteristics were evaluated with attention to the phospholipid

and protein adsorptions, and platelet adhesion. In this study, in order

to evaluate an availability of the MAPC copolymers as coating materials for poly(vinyl chloride)(PVC), which is commonly used in extra

corporeal circuit, such as tubing, reservoirs, connectors etc, hemocompatibility of PVC coated with MAPC copolymer was evaluated through in vitro tests and ex vivo shunt expts. When platelet-rich plasma (PRP) was contacted with PVC for 60 min, a lot of

platelets adhered and activated, On the MAPC copolymer of 0.1 MAPC mole fraction, the number of platelet adhered decreased with an

increase in the methylene chain length. On the other hand, when MAPC mole fraction was increased to 0.3, platelet adhesion was completely suppressed. The similar tendency of the platelet adhesion with

respect to the methylene chain length was observed when PRP was contacted

with the surface of poly (BMA) coated with MAPC copolymer of 0.1 mol fraction for 180 min. Regarding the ex vivo tests, carotid artery-venous shunt expts. were carried out using rabbits and it was

confirmed that after 30 min' circulation, a lot of platelets adhered on

the MAPC coated PVC surface compared with the results obtained in vitro tests. But the number of platelet adhered also decreased with an

increase in the methylene chain length.

STN

DUPLICATE 13

AN 1994:494318 BIOSIS

DN PREV199497507318

TI Effect of methylene chain length in phospholipid moiety on blood compatibility of phospholipid polymers.

AU Iwasaki, Y.; Kurita, K.; Ishihara, K. [Reprint author]; Nakabayashi, N.

CS Inst. Med. Dent. Eng., Tokyo Med. Dent. Univ., 2-3-10, Kanda-surugadai, Chiyoda-ku, Tokyo 101, Japan

SO Journal of Biomaterials Science Polymer Edition, (1994) Vol. 6, No. 5, pp. 447-461.

CODEN: JBSEEA. ISSN: 0920-5063.

DT Article

LA English

ED Entered STN: 28 Nov 1994

Last Updated on STN: 29 Nov 1994

AB To investigate the effects of the methylene chain length between the

phospholipid polar group and the backbone on blood compatibility of a

phospholipid polymer, copolymers of omega-methacryloyloxyalkyl phosphorylcholine (MAPC) with n-butyl methacrylate (BMA) were synthesized. The methylene chains were ethylene (n = 2), tetramethylene

(n = 4), and hexamethylene (n = 6). Every MAPC copolymer with an MAPC mole fraction in the range of 0.1-0.3 was soluble in ethanol but only swelled in water, and the equilibrium water fraction of

the water-swollen MAPC copolymer membrane decreased with the length of the methylene chain. When a rabbit platelet-rich plasma was

applied on the MAPC copolymer surface with an 0.1 MAPC mol fraction for 180 min, the number of adhered platelets depended on the

length of the methylene chain in the MAPC moiety of the copolymer. The amount of phospholipid adsorbed on the MAPC copolymer from human plasma was larger than that on hydrophobic poly(BMA)

and increased with the length of the methylene chain in the MAPC moiety. That is, the reduction of platelet adhesion corresponded to the

increase in the amount of phospholipid adsorbed on the MAPC copolymer.

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DUPLICATE 14

AN 1994:276227 BIOSIS

DN PREV199497289227

TI Effects of 4-MAPC, a 5-alpha-reductase inhibitor, and cyproterone acetate on regrowth of the rat ventral prostate.

AU Shao, Tsang C.; Kong, Ann; Cunningham, Glenn R. [Reprint author]  
CS ACOS Res. and Dev., VA Med. Cent., 2002 Holcombe Blvd., Houston,  
TX 77030,  
USA  
SO Prostate, (1994) Vol. 24, No. 4, pp. 212-220.  
CODEN: PRSTDS. ISSN: 0270-4137.  
DT Article  
LA English  
ED Entered STN: 24 Jun 1994  
Last Updated on STN: 25 Jun 1994  
AB Inhibitors of 5-alpha-reductase activity cause less involution  
of the rat  
ventral prostate (VP) than does castration. Studies were  
conducted in  
adult Sprague Dawley rats to evaluate the effects of a potent  
5-alpha-reductase inhibitor, 4-MAPC, and the antiandrogen,  
cyproterone acetate (CA), on DNA synthesis and apoptosis. In  
experiment  
1, VP weight fell 33%, 53%, and 83%, and DNA per ventral  
prostate was  
reduced 24%, 46%, and 71%, by 4-MAPC, CA, and castration,  
respectively. In experiment 2, adult rats were castrated, and  
the VP  
involved for 7 days prior to 3 daily injections of testosterone  
propionate (TP; 1 mg/kg/d) +/- 10 mg/kg/d of 4-MAPC or CA.  
3H-thymidine incorporation into VP DNA was increased in  
castrated animals  
treated with TP, and 4-MAPC and CA reduced uptake. In  
experiment 3, animals were treated for 14 days with the same  
protocol as  
that used in experiment 2. VP weight was increased in all  
animals treated  
with TP when compared with castration, and was reduced by both 4-  
MAPC and CA. DNA in rats treated with TP was similar to that in  
intact animals. DNA was not reduced by 4-MAPC, but was reduced  
by CA. The mRNA for TRPM-2, a marker of apoptosis, was  
increased only in  
untreated castrated rats. It appears that CA has a greater  
inhibitory  
effect than 4-MAPC on DNA synthesis. A major reason why  
castration reduces DNA more than either 4-MAPC or CA is that  
neither of these agents was able to increase programmed cell  
death to the  
degree seen with castration.

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DUPLICATE 15

AN 1994:364562 BIOSIS  
DN PREV199497377562

TI Correlation between some lipophilicity characteristics of  
morpholinoethylesters of 2-, 3- and 4-alkoxysubstituted  
phenylcarbamic

acids, and their inhibitory activity in photosynthesizing organisms.

AU Kral'ova, K.; Loos, D.; Cizmarik, J.

CS Inst. Chem., Fac. Nat. Sci., Comenius Univ., 842 15 Bratislava, Slovakia

SO Photosynthetica (Prague), (1994) Vol. 30, No. 1, pp. 155-159.  
CODEN: PHSYB5. ISSN: 0300-3604.

DT Article

LA English

ED Entered STN: 23 Aug 1994

Last Updated on STN: 23 Aug 1994

AB Morpholinoethylesters of 2-, 3- and 4-alkoxysubstituted phenylcarbamic

acids (MAPC) inhibit photosynthetic processes in algae and plant chloroplasts. The inhibitory activity of MAPC in photosynthesizing organisms was in good correlations with lipophilicity

characteristics such as hydrophobic fragment constants, partition coefficients and chromatographic retention factors.

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NEWS	14	FEB 23	TOXCENTER updates mirror those of MEDLINE - more precise author group fields and 2009 MeSH terms
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			STN patent clusters
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